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THE PROGNOSTIC VALUE OF THE HISTOLOGICAL MALIGNANCY INDEX AND THE CLINICAL GROUPING OF CARCINOMATA OF THE UTERINE CERVIX[1]

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IN 1926 the preliminary results of a study on the significance of the "Histological Malignancy Index" for the prognosis and treatment of carcinomata of the uterine cervix were published by us (1, 2). The histopathology of 139 cases of cervical carcinomata was studied, observing and evaluating nine factors, namely: the special cell type; the irregularity in the size and shape of the cell and nucleus; the distinctness in the outline of the cell; the functional activity of the cell; the hyperchromatism of the nucleus; the number of mitoses and prophases. The details of the determination of the numerical values were also given in the report. Of the 139 cases the end-results were known in 58 cases. The latter were used to establish the relation of the histological malignancy index to the prognosis and treatment. The malignancy index values ranged from 10 to 40 and were arranged in four groups from 10 to 20, 21 to 25, 26 to 30, and 31 to 40. The percentages of good end-results for these histological malignancy index groups were 61.54, 42.85, 27.27, and 0, respectively. Carcinomata with a histological malignancy index of 31 or higher usually have a bad prognosis.

The carcinomata were also graded according to the extent of the growth, as determined by physical examinations, and assigned to one of four groups. A survey of the cases treated up to five years ago was made at the same time. The number of carcinomata was 183 and the percentages of five-year good end-results in the clinical groups was 80.0, 33.33, 11.8, and 0, respectively. Carcinomata characterized by fixation of the growth were assigned to clinical Group 4 and invariably gave a poor prognosis.

The conclusion drawn from these observations was that a cancer with a histological malignancy index higher than 30 and belonging to the histological malignancy Group 4, or a fixed cancer assigned to clinical Group 4, gives a bad or infaust prognosis.

The pathological and clinical investigations have been continued—the former comprise at present 227 cases with 100 known end-results, and the latter include 332 cases, of which 58 have passed a five-year period free from subjective and anatomic evidences of the disease.

An interesting fact was brought to light in these investigations. The studies on the distribution of the intensities of rays in the water phantom, initiated by Friedrich, the construction of the modern high voltage

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transformer, and the perfection of the Coolidge tube have led to a progressive change in the technic of radiation therapy. This, in turn, has brought about a marked increase in the good five-year end-results.

The results of the investigations on the histological malignancy index, the clinical groups, and the comparison of five-year cures obtained with the modern high voltage X-ray therapy in combination with radium, with those obtained with the former low voltage X-ray therapy are herewith given.

A review of the literature has not been given. It may be found in the references given at the end of this treatise.

THE DETERMINATION OF THE HISTOLOGICAL MALIGNANCY INDEX

The study of the histopathology of the present series included four main factors: (1) the special cellular characteristics; (2) the characteristics of the cytoplasm; (3) the characteristics of the nucleus, and (4) the characteristics of the stroma (3, 4). Table I is a reproduction of the first page of our journal. It shows the various factors investigated in each of the main divisions.

It would consume too much space and time to enter into detailed discussion of the determination of the numerical value for each of the subfactors. A few examples may suffice.

Special Cell Type of Carcinoma.—The carcinomata were grouped according to their general structure and predominant cell type into two main groups: the primary solid and the tubular or glandular carcinomata. Each main group was again divided into four subgroups to which definite numerical values were given.

A. Primary solid carcinomata:
  1. Spinous cell carcinoma with cornification
     Value 1
  2. Spinous cell carcinoma without cornification
     Value 2
  3. Round cell carcinoma
     Value 3
  4. Spindle cell carcinoma
     Value 4

B. Glandular carcinomata:
  1. Malignant adenoma
     Value 1
  2. Papillary and gelatinous adenocarcinoma
     Value 2
  3. Adenocarcinoma simplex
     Value 3
  4. Solid adenocarcinoma
     Value 4

TABLE I

Journal number histological malignogram	1	2	3	4	5	6	7
1. Special cellular characteristics: Value 4–16							
a. Special cell type	4	3	A4	3	2	3	3
b. Nucleo-cytoplasm ratio	4	4	4	1	4	4	1
c. Pencil cells	4	4	4	4	1	1	3
d. Infiltrative growth	3	2	3	1	1	4	2
2. Characteristics of cytoplasm: Value 5–20							
a. Irregular size of cells	2	2	4	3	4	1	4
b. Irregular shape of cells	4	3	4	2	4	1	4
c. Distinctness cell outline	4	4	4	2	2	4	4
d. Chromatism of cytoplasm	3	3	4	1	1	4	2
e. Functional activity of cells	4	4	4	4	1	4	3
3. Characteristics of nuclei: Value 6–24							
a. Irregular size of nuclei	4	3	3	4	4	2	4
b. Irregularity in shape	4	2	3	3	4	1	4
c. Chromatism of nuclei	4	4	3	2	4	4	3
d. Hyperchromatism	4	4	4	4	4	1	4
e. Number of mitoses and prophases	4	3	4	3	4	4	2
f. Irregularity of mitoses	3	2	4	1	4	4	3
4. Characteristics of stroma: Value 5–20							
a. General type of carcinoma	3	4	4	4	3	4	2
b. Character of stroma	2	4	3	3	2	2	4
c. Vascularity of stroma	3	4	4	4	3	3	4
d. Type of cellular infiltration	3	3	2	3	3	2	3
e. Amount of cellular infiltration	3	1	1	2	2	2	3
Malignancy index	69	63	70	54	57	55	62
Clinical group	3	3	R3	R3	3	3	4
Clinical end-result	4		4	3	3	1	2

Irregularity in Size and Shape of Cells.—The average size and shape of the tumor cells were studied. Deviations from the average size or shape present in 40 to 50 per cent were valued 4 points; 30 to 40 per cent, 3 points; 20 to 30 per cent, 2 points, and less than 20 per cent, 1 point.

Hyperchromatism of the nuclei was determined by comparison with the intensity of the stain of the nuclei in the lymphocytes. If 20 per cent of the nuclei were hyperchromatic, the value 4 was given; 15 to 20 per cent were valued 3 points; 10 to 15 per cent, 2 points, and less than 10 per cent, 1 point.

General Type of Carcinoma.—If the parenchyma of the tumor was 75 per cent or more and the stroma 25 per cent or less, the value 4 was given. If the parenchyma was 50 to 75 per cent and the stroma 25 to 50 per cent, 3 points were given. If the parenchyma was 25 to 50 per cent and the stroma 50 to 75 per cent, 2 points were counted. And if the parenchyma was 25 per cent or less and the stroma 75 per cent or more, the value 1 was given.

The number of histological malignancy indices was 227. Table II is a tabulation of the malignancy indices for each cell type.

TABLE II

Cell type	Range of malignancy index	Average malignancy index	Number of cases
Ad. 1	40–45	42.5	2
Ad. 2	43–61	50.7	10
Ad. 3	47–64	53.7	24
Ad. 4	47–79	62.8	25
			— 61
S. 1	39–62	49.6	8
S. 2	34–70	50.8	52
S. 3	41–73	58.1	83
S. 4	45–76	65.7	25
			— 168

Ratio 27.54 : 72.46

The range of the malignancy indices in each cell type precludes the possibility of using the cell type alone in the determination of the degree of histological malignancy.

THE CLINICAL GROUPING OF CARCINOMATA

The clinical grouping is based on the physical findings (5). The carcinomata are divided into primary and secondary or recurrent. The factors which determine the grading of the primary carcinomata are:

Group 1 signifies a cancer growth clearly localized within the cervix. It should be about 1 cm. in diameter. The size is determined by palpation and inspection. The genital organs are movable within normal limits.

Group 2 indicates a growth which has extended to the periphery of the cervix in a longitudinal or transverse direction. The uterus has an impeded movability due to a dough-like consistency and decreased elasticity of the paracervical tissues.

Group 3 means that either one or both parametria or regional lymph groups have been invaded, a fact which is elicited by rectal examination. The tumor mass is movable though elasticity of the tissues is lost.

Group 4 includes the carcinomata with absolute fixation.

The characteristics of the groups in the recurrent carcinomata are: *Group R1* contains the local but normally movable recurrence; *Group R2* the regional but movable recurrence; *Group R3* the cases with local and regional movable recurrences, and *Group R4* the recurrence with fixation of the mass.

The clinical grouping has a threefold purpose. It indicates those cases which invariably have a poor prognosis. It is also an aid in establishing exact statistics to determine the therapeutic efficacy of either operation or radiation in cervical carcinomata. Such expressions as "operable," "borderline," and "inoperable" cases lead to confusion. The designation of operability and inoperability must of necessity vary with each individual, depending on the ex-

TABLE III

Journal number	1	3	4	5	6	7	8	9	10	11	14	15	16	17	21	22	24	25	29	30
Malignancy index	69	70	54	57	55	62	54	63	65	64	67	47	61 Ad	51 Ad	52	53	56	67	53	58 Ad
Clinical group	3	R3	R3	3	3	4	3	4	3	2	R3	2	R1	R3	R4	2	3	2	3	3
End-result	4	4	3	3	1*	2	3	4	2	4	3	1	1*	4	4	2	3	4	1	2
Journal number	31	33	35	37	40	41	45	46	47	48	49	51	52	53	55	57	58	61	62	63
Malignancy index	66	52	54	37	64 Ad	49	62	47	49 Ad	64	40	75 Ad	64	62	61	52	55	50	55	38
Clinical group	R3	R4	4	4	R4	3	3	3	3	3	3	3	3	4	4	3	4	3	2	R3
End-result	3	1	3	4	4	1*	3	1*	1*	3	1*	3	2	4	4	1	4	1*	1	2
Journal number	65	66	68	70	71	72	73	74	76	77	78	79	83	85	86	87	89	90	92	93
Malignancy index	72	47 Ad	45	56	47 Ad	56	53	64	62	63	57	74	41	61	57	41 Ad	66	44	54	44
Clinical group	3	3	4	3	2	2	3	3	4	3	3	4	3	4	4	4	4	3	4	2
End-result	3	1	3	4	3	1	3	1*	3	3	1	4	1	4	1	4	4	1	3	1
Journal number	95	96	98	99	100	107	111	118	121	122	131	149	175	176	177	178	179	180	181	182
Malignancy index	54	45 Ad	49	52 Ad	45	46	68	60	49	55	63	59	55 Ad	62 Ad	45	64	65	39	67	54
Clinical group	4	1	R4	4	R3	1	3	4	3	4	1	2	1	R3	4	3	3	4	4	3
End-result	1	1	3	3	3	1	2	4	2	4	1	4	1	3	4	3	3	2	2	1
Journal number	184	185	186	187	189	190	192	194	195	198	199	201	202	205	206	208	210	217	218	222
Malignancy index	62	61 Ad	57 Ad	62 Ad	66 Ad	60	49 Ad	55 Ad	48 Ad	53	52	60	64	61	47	45	49	59	50	48
Clinical group	2	2	3	4	4	4	4	2	R3	4	2	4	3	3	4	4	4	3	R3	4
End-result	1	1	2	4	4	3	2	4	2	4	1	4	1	4	4	2	4	4	1	4

perience and skill of the surgeon. The method of clinical grouping evolved by us avoids such discrepancies. "Clearly localized," "doubtfully localized," "advanced," and "terminal" or "fixed" cancers have definite meaning.

Lastly, the clinical grouping enables one to determine the correct indications for treatment. *Group 1* indicates either surgery or radium therapy, *Group 2* and *Group 3* indicate radium and X-rays, and *Group 4* palliative treatment. *Group R1* indicates radium; *Group R2*, X-rays; *Group R3*, radium and X-rays, and *Group R4*, palliation.

Should Groups 4 and R4 improve unexpectedly under proper treatment, then one must assume that the fixation was probably of an infectious nature and combined radium and X-ray therapy is then applied.

THE PROGNOSTIC VALUE OF THE HISTOLOGICAL MALIGNANCY INDEX

The prognostic value of the histological malignancy can be established only by a comparison of the latter with the known end-results. For this purpose all the cases in which the end-results were known were extracted from the journal. Table III is a tabulation of the 100 cases with known end-results. The first line gives the journal number, the second line the malignancy index, the third line the clinical group, and the fourth line the end-results. The cases belonging to the

glandular carcinomata are indicated by an "Ad" underneath the malignancy number. The recurrent carcinomata are designated by an "R" before the clinical group number. An asterisk (*) after the end-result means that the patient has passed a five-year period free from cancer.

"Clinical end-result 1" means that the patient was free from symptoms and showed anatomical healing three years after termination of the radiation treatment. "End-result 2" indicates exitus during the third year; "end-result 3," during the second year, and "end-result 4," during the first year after treatment. (See Table IV, page 366.)

THE RELATION OF THE MALIGNANCY INDEX AND CLINICAL GROUP TO THE END-RESULT

Table IV has been prepared from Table III. It contains the 100 cases with known end-results arranged according to the malignancy index, the known end-result, and the clinical group. The average of the malignancy indices is 55.78, or practically 56, and is indicated by a heavy line. Interrupted lines have been arbitrarily placed above and below at 68 and 44, which are +12 or —12 from 56. Cases above 68 probably give a poor prognosis. There are 23 cases, or 74.19 per cent, with end-result 1 below, and 8 cases, or 25.81 per cent, with end-result 1 above the average line at 56.

In determining the relation of the histological malignancy index to the prognosis the clinical Group 4 cases should be eliminated, as they almost always give a poor prognosis regardless of the histological malignancy index. The percentage of good end-results to the entire number of cases within each histological group is shown in Table V (see this page).

The percentages of the end-results obtained in the histological and clinical groups may be plotted as seen in Figure 1, which is self-explanatory. If a straight line is drawn from 0 in Group 4 to 79 in Group 1, which values present the averages of the histological and clinical percentages, then the intersections with the ordinates give the range of end-result 1 percentages probably attainable in the respective histological and clinical groups. Therefore the straight graph has been termed the "malignancy line."

DISCUSSION

The prognosis of a carcinoma depends upon numerous factors. These may be inherited or acquired, permanent or transient, local or general. The factors may be considered under five divisions:

1. The degree of the histological malignancy of a carcinoma as represented by the infiltrative, destructive, and histologic qualities of the tumor cells and of the stroma. The factors form the basis of the histological malignancy index.

2. The extent of the tumor depends to some degree on the duration of the disease and the infiltrative intensity of the growth. It forms the basis of the clinical grouping.

3. The endogenous carcinolytic power and protective resistance of the host, which probably depends on age, race, sex, constitution, heredity, and so forth. These factors have been investigated to some extent by one of us (6).

4. Exogenous factors, that is, the chronic irritation produced by external agencies,

TABLE V

Malignancy index	32 to 44	45 to 56	57 to 68	69 to 80
Total number of cases	5	28	27	2
Number end-result 1	4	17	7	0
Percentage end-result 1	80.0	60.71	25.82	0.0

TABLE IV

Malignancy index	End-result 1. Clinical group				End-result 2. Clinical group				End-result 3. Clinical group				End-result 4. Clinical group			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
37																1
38							R									
39								1								
40			1													
41			1													
42																
43																
44		1	1													1
45	1							1			R	1				1
46	1															
47		1	2				1									1
48							R									1
49			2				1	1				R				1
50			1R													
51																R
52		1	1	R								1				R
53			1								1					1
54			1	1							R1	1			1	1
55	1	1	1											1		1
56		1									1				1	
57			1	1			1				1				R	
58							1									
59												1		1		
60												1				2
61	R	1													1	2
62		1						1			1R				1	2
63	1										1					1
64			2				1				2			1		R
65							1				1					
66											R					2
67								1			R			1		
68							1									
69															1	
70															R	
71																
72											1					
73																
74																1
75											1					
76																
77																
78																
Total Number	5	7	16	3			9	5			16	6		4	7	22

such as tar, paraffin, aniline dyes, radiations, chemicals, bacteria, parasites, trauma, and so forth.

5. Secondary complications by the neoplasm. They are: (*a*) Mechanical causes, as pressure and obstruction of glandular ducts, ureters, intestines, esophagus, etc.; (*b*) Secondary infections of the tumor and surrounding tissues, which decrease general resistance and may prove fatal; (*c*) Toxemias from resorption of toxic products of necrotic tumors.

It is obvious that all these factors should be evaluated in rendering a prognosis in a given instance. The "histological malignancy index" and the "clinical group" are important aids in the prognosis. The surgeon and radiologist will have to consider them in choosing the indicated method of treatment. A clinical Group 4 carcinoma and a carcinoma with a histological malignancy index of 68 or higher give each an infaust prognosis. Such cases should not be subjected to a needless operation or a useless radiation treatment. The parallelism of the graphs of the percentages of the five-year end-results and the malignancy index groups is convincing evidence of the value of such grading (see Fig. 1).

THE FIVE-YEAR END-RESULTS OBTAINED WITH RADIUM AND X-RAYS OF VARYING VOLTAGES

Carcinomata of the uterine cervix we have always treated with a combination of radium and roentgen rays. Our technic of radium applications, which we have never changed, consists of the intracervical insertion of two 25 milligram element capsules of radium placed in a metal filter of 0.5 mm. silver and 1.5 mm. brass. The radium applications are made in three weekly intervals of 30 to 32 hours' duration.

The technic of roentgen treatment has been changed with the development of the transformers and the X-ray tubes. Three periods were observed.

The kilovoltage has been subjected to frequent controls with a sphere gap measure, an electrometer standardized by Bachem in German *r*-units, and a Seamann spectrograph.

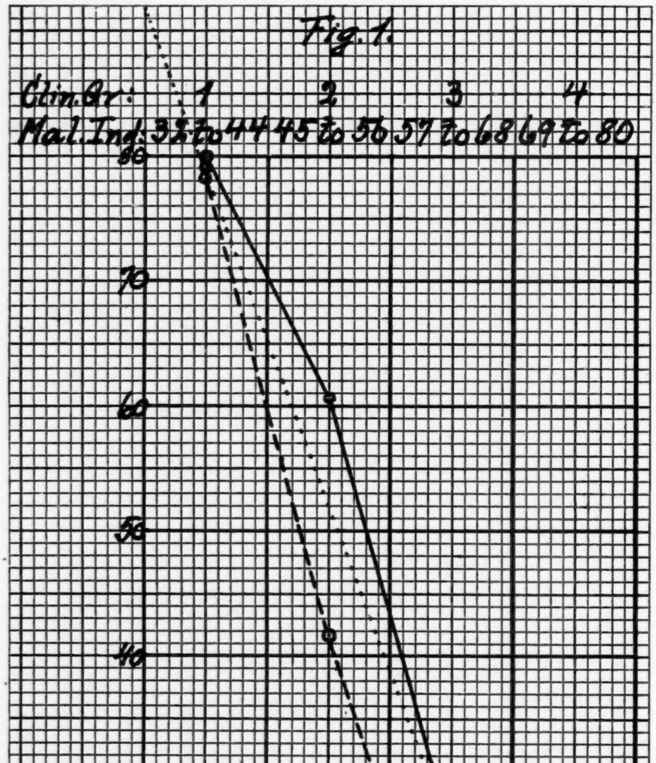
Table VII (page 369) gives the percentage of cases free from cancer at the end of five years.

The short wave X-ray therapy has increased the five-year cures in clinical Group 3 to 18.65 per cent, while with the long wave technic they were 9.21 and 7.69 per cent. Radium rays cannot effectually arrest a carcinoma in the parametria or at the bony pelvic girdle, the seat of the regional lymph nodes. A 50 mg. el. radium capsule inserted in the cervical canal from 48 to 96 hours attains an intensity at 6 cm. of 12.5 to 25 per cent of an erythema skin dose.

The recurrent carcinomata numbered 138 with 5 five-year good end-results in Group

TABLE VI

Factors	1914 to 1919	1920 and 1921	1922 and 1923
Kilovoltage peak	110	140	211
Milliamperes	5	5	25
Target skin distance	25–30 cm.	65 cm.	65 cm.
Size of fields	5 cm. sq.	15 cm. diam.	15 × 20 cm.
Number of fields	10 to 20	2 to 4	2 to 4
Filter	4 mm. Al. plus 1 sole leather	0.5 mm. Cu.+ 1.0 mm. Al.	0.75 mm. Cu.+ 1.0 mm. Al.
Dose at depth of 10 cm.	About 20%	About 30%	About 48%
Time duration application	150 min. per field	1050 min. per field	1000 min. per field
If applied within five 4-day intervals			1375 min. per field
Approximate German *r*-units			800 *r*-units
Intervals between treatments	1 field daily	1/3 dose daily to a field	



Graphs of Percentages of End Results in Clinical and Histological Gradings. Continuous Line = Malignancy Index. Interrupted Line = Clinical Groups. Dotted Line = Malignancy Line.

R1, or 50 per cent—an absolute cure of 5.79 per cent for the entire number. Unless recurrences are local and movable, *i.e.,* belong to Group R1, a good end-result cannot be expected from radiation treatment.

It may be concluded that the modern short wave X-ray therapy has increased the number of good results at the end of five years. The number increased from 14.02 per cent in the first period to 18.18 per cent in the second period, and to 20.32 per cent in the third period.

SUMMARY

The technic of the evaluation of the histological malignancy index for cervical carinomata has been given.

A tabulation of 100 malignancy indices with known end-results has been made. The good end-results diminish in number with an increase in the values of the malignancy indices. An index higher than 68 indicates an infaust prognosis.

The five-year end-results of 332 cases of primary and 138 cases of recurrent cervical carcinoma treated with radiations have been tabulated into four clinical groups. The Group 4 cases give an invariably bad prognosis.

The percentages of five-year end-results obtained in each clinical group, and of good

TABLE VII

	1914–1919	1920–1921	1922–1923	Total
Group 1				
Number of cases	5	9	9	23
Number 5-year cures	5	6	7	18
Percentage 5-year cures	100.0	66.67	77.78	78.27
Inconclusive cases		3		
Group 2				
Number of cases	16	13	19	48
Number 5-year cures	7	6	7	20
Percentage 5-year cures	43.75	46.75	36.84	41.68
Inconclusive cases	3	5	10	
Group 3				
Number of cases	76	26	59	161
Number 5-year cures	7	2	11	20
Percentage 5-year cures	9.21	7.69	18.65	12.42
Inconclusive cases	26	13	20	
Group 4				
Number of cases	35	29	36	100
Number 5-year cures	0	0	0	0
Percentage 5-year cures	0	0	0	0
Inconclusive cases	12	17	15	
Percentage of 5-year cures in each period	14.02	18.38	20.32	17.50

end-results obtained in the histological malignancy index groups, have been plotted. The graphs run an almost parallel course and approach the ideal of the "malignancy graph," which is a straight line. The intersection of the malignancy graph with the ordinates indicates the probable range of percentages of good end-results in each group.

The factors influencing the prognosis of carcinomata have been briefly discussed.

The short wave roentgen-ray therapy has brought about a remarkable increase in the number of the five-year good end-results in comparison to those obtained with the long wave X-rays. As the radium dose remained the same in both technics the higher percentage of five-year good end-results must be ascribed to the action of the short wave X-rays.

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THE CHEMICAL AND BIOLOGICAL CHANGES INDUCED BY X-RAYS IN BODY TISSUES[1]

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THE object of a series of experiments which we have been carrying on during the last several years has been to throw light on the general biological action of X-rays. While much work has been done on the immediate effects of these rays on cells of various kinds, little has been learned about the chemical effects induced by them in the organism. One striking fact that has been the outcome of the general studies of X-rays and which promises an eventual solution of this problem when more has been learned about cellular growth in the organism and cancer, is that X-rays are not only able to destroy cancer cells, but may induce cancer. Another equally important fact is that growing cells are more sensitive to these rays than the more differentiated tissue.

In the light of these various facts it has become evident, therefore, that X-rays will be understood only when we understand cancer, and every advance in the knowledge of cancer must throw further light upon the nature of the action of these rays. As early as 1775 Potts had already noticed a relation between soot and cancers of the scrotum in chimney sweeps. More recently Yamagiwa and Ishikawa have proved that repeated doses of coal tar will induce cancer in rabbits. Many confirmations of these experiments have shown very definitely that cancers can be induced not only by repeated applications of coal tar, but many other lipoid solvents. It became evident, therefore, that the fundaments of X-rays and cancer lay hidden in the final analysis of the action of coal tar, soot, and other lipoid solvents upon the tissues.

Analyzing X-rays in terms of truths learned from the study of the action of lipoid solvents, we have noted certain facts which indicate that their chief action is a disturbance of the balance of vitamins in the body. It becomes of interest, then, in this article to review this early work on X-rays, to relate experiments which led up to those with X-rays, and to describe others which have strengthened this viewpoint.

In the tissue culture it was noticed that the yolk-laden blastomeres of the egg will not grow in a plasma culture unless stimulated by the addition of the growth-stimulating substance, the archusia. This inability of the blastomeres to grow independently disappears with the disappearance of the yolk granules within them. Subsequent to this period the progeny of these same embryonal cells grow readily and independently in hanging drops of plasma in the tissue culture.

By testing fragments of the same embryonic tissue of various ages it was noted that only the cells of young embryos grow with great ease in the plasma culture. As the embryos grow older these same cells grow with less and less vigor and finally cease to grow in the plasma unless they are washed by several changes of plasma, benzol, or other lipoid solvents. This loss of the power to grow makes its appearance with the development of cell membranes and intercellular substances in the embryo and young animals.

[1]Presented before the Thirteenth Annual Meeting of the Radiological Society of North America, at New Orleans, Nov. 29, 1927.

From these observations we were forced to believe that the inhibition of growth in early embryonic life and in the later period is associated with the presence of the yolk granules in one case and the presence of the intercellular substances in another. The studies of the effect of lipoid solvents on relieving the inhibition for independent growth in the adult tissue indicate further that this inhibition is due also to the presence of lipoid substances in the intercellular materials.

In attempting to throw further light upon this question the general composition and manner of absorption of the yolk and the formation and composition of the intercellular substances has been analyzed (2). These analyses have shown that the absorption of granules by the cells is accomplished through the absorption of a lipoid substance (the ergusia) by the protein and fat parts of these granules (1). The basic substances of the connective tissue fibrils and other intercellular substances are proteins coagulated by the ergusia (1) (2). The ergusia is either the same or is formed from those fat-soluble vitamins of the food which are necessary for the proper growth and development of the organism (3).

These facts show very clearly that the mechanism of the action of coal tar and other lipoid solvents in the production of cancer is that they are able to remove the excess of lipoid-soluble elements from about the cells in the tissues.

The observations of all authors studying the action of oils and coal tar have shown also that these substances act only to induce cancer. The cancer, once induced, proceeds then, always independent of them.

It had become evident to us, therefore, that X-rays must act also in the same capacity in inducing and destroying cancer. To prove this point it had become necessary for us to look more carefully into the general nature of this lipoid substance (ergusia) and the nature of the water-soluble stimulating substance (archusia). These latter studies have shown very definitely that the water-soluble archusia is probably very similar to, or the same as, Vitamin B of nature (4), and that the ergusia, or the lipoid substance, is the same as or is derived from that group of fat-soluble vitamins which are necessary for the growth of the body (3). It became possible, therefore, to throw light upon this subject through a study of the effect of these rays on animals fed on various dietaries which are either deficient in or contain ample proportion of these vitamins (5).

Another method of studying the effect of these rays was a careful histological comparison of the changes in the tissues induced by coal tar and other lipoid solvents and those induced by X-rays.

Before we could undertake any of these studies it was necessary to be able to use known doses of X-rays in each case. Ernst (6) had already made a study of means to measure the doses of these rays. In all of these experiments carefully measured doses have been used according to his technic.

HISTOLOGICAL CHANGES INDUCED BY X-RAYS, COAL TAR AND OTHER LIPOID SOLVENTS

Jorstad and Lane (7) treated many areas of the skin of rats with graded doses of X-rays. While these animals are probably much less sensitive to the effects of X-rays and the various lipoid solvents than mice, their greater resistance probably has made them more valuable for an analysis of the more minute changes of the sublethal doses. Excellent and ample material has thus been collected for histological study.

Jorstad and Johnston have also studied the effect of coal tar as well as many vegetable, animal, and mineral oils and fats. These various substances have been injected

as well as applied superficially. They have been left in the body for various periods of time and then removed and their histological effects determined (8) (9) (10).

Since Jorstad and his co-workers have described these lesions, or are describing them in detail, we will give only a general summary of their results at this time.

As noted in these papers (8) (9) (10), drops of coal tar placed in the tissue cause, first, a rapid migration of fibroblasts, the endothelial cells of the blood vessels, and epithelial cells to them. These cells become crowded around the periphery of the drops of coal tar. In cellular tissue the first cells to reach the drops of coal tar degenerate. The later ones survive, and, if crowded sufficiently, grow. In a less cellular tissue, growth does not intervene, but the whole becomes transformed into a hyaline mass. In the skin the epithelial cells show growth with small doses of coal tar, while the less cellular connective tissue becomes reduced rather readily to a hyaline tissue.

Larger doses of coal tar cause extensive early degeneration, with later regenerative recovery in a cellular tissue. The smaller doses always cause extensive hyaline changes in the connective tissue.

As one of us has pointed out (2), these hyaline changes may be interpreted as the result of the loss of the ergusia or the lipoid elements of the tissue as the growth may be likewise interpreted.

A study of the action of X-rays has given exactly the same result. Small doses of X-rays applied to the skin cause a definite hyperplasia of the more cellular epidermis, with accompanying hyaline changes in the connective tissue or derm. Larger doses cause necrosis of the epidermis, with a more extensive degeneration of the connective tissue fibrils, the blood vessels, and lymphatics of the dermis.

If the effect of the coal tar is to remove the lipoid elements of the tissue, there is no evidence from any of these observations that X-rays do not act also in the same capacity.

EFFECTS OF X-RAYS ON ANIMALS FED VARIOUS DIETARIES

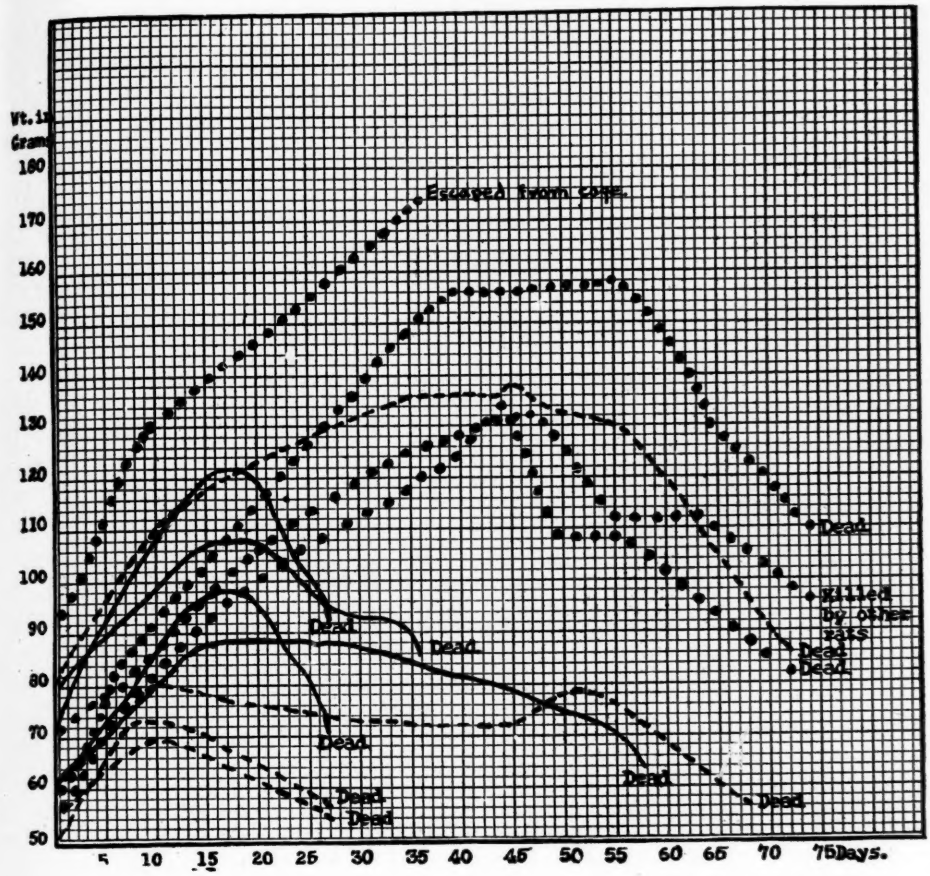
In several papers before this Society we have reported our observations on the differences of the effect of definite doses of X-rays on animals fed on different dietaries (5) (11) (12).

As noted in the previous experiments, we found that small doses of X-rays, 10 milliampere minutes (13 *e*-units), given twice a week, protect rats for a time against a dietary deficient in Vitamin B, but have little effect on rats fed on a dietary deficient in Vitamin A.

Slightly larger doses, 25 and 50 milliampere minutes (34 and 68 *e*-units, respectively), act differently in that they protect the rats not only against a dietary deficient in Vitamin B, but also against a dietary deficient in Vitamin A. The rats in both instances not only lived from two to three times as long as the controls, but grew normally for a period as great as a hundred days. The rats given only the dietary deficient in Vitamin A often showed no growth after the first five to ten days.

These results were quite comparable to those obtained with coal tar. Jorstad (13) finds that one to three cubic centimeters of coal tar injected subcutaneously into an 80-gram rat living on a dietary deficient in Vitamin A, causes an immediate loss of weight, and death in a few days. Similar rats given a dietary rich in Vitamin A suffer only a temporary drop in their growth-curve when given 8 to 10 cubic centimeters of coal tar subcutaneously.

The coal tar dissolves and removes the lipoid substances from the tissues. Lights, on the other hand, as is well known, liberate Vitamin A from animal and vegetable fats and tissues so that they become available



—— diet of dog biscuits
- - - - diet of dog biscuits and milk
. . . . diet of dog biscuits, milk, and cod liver oil

X-ray dose, 136 *e*-units twice a week.

Fig. 1. Growth curves of rats fed the various dietaries noted above and given 100 milliampere minutes of X-rays (136 *e*-units) twice a week.

for use by animals. There is no evidence that X-rays destroy these fat-soluble vitamins. Their whole action, as noted from the above experiments, is an evident liberation of them from certain tissues so that they become available to others. When the small doses are given one might assume that the rays are largely absorbed in the superficial layers. If this be true, the rats should grow normally for a time and then die suddenly as these tissues become exhausted.

In further proof of this belief it is noted that larger doses—75 milliampere minutes and 100 milliampere minutes (102 and 136 *e*-units, respectively)—cause a rapid loss of weight and death within ten days in rats fed a dietary deficient either in Vitamin B or Vitamin A. When both of these vitamins are present (yeast and butter fat) in the diet, the animal survives for a considerable time.

DIETARY IN THE TREATMENT OF CANCER

These latter facts in reference to the protection of butter fat and a proper amount of Vitamin B against lethal doses of X-rays,

were interesting to investigate further on account of their possible value in treatment.

It has been customary for a long time to use dog biscuits as a regular basic diet for our breeding colony of rats. It was found after using them for a time that the rats did not do very well unless we gave fresh meat, a certain amount of corn or wheat, and carrots or lettuce. It became of interest to see, therefore, what might be the effect of the X-rays on rats fed on these biscuits alone, and on these biscuits with milk added in one case, and cod liver oil in another. The results of one of these experiments is given in Figure 1. In this series of experiments all of the rats did not drink the milk well. These rats were given two bottles, one containing fresh certified milk and the other bottle containing water. The cod liver oil was given by mixing it with ground dog biscuits and feeding this mixture with water as the entire diet. Five cubic centimeters of pure cod liver oil was added to enough ground dog biscuit to feed the four rats for ten days. In the cages where milk was given, only one rat drank the milk. It is interesting in looking over the results to see, therefore, the striking effect of milk and cod liver oil in protecting these animals against the rays. All rats living on the dog biscuits alone succumbed rather quickly, while those given either cod liver oil or milk survived for a considerable time.

In other repetitions of this experiment we succeeded in getting the rats adapted to milk before the experiment was started. In these experiments one sees little difference in the resistance of rats fed milk as compared with those fed with cod liver oil.

In other experiments it became of interest, then, to test the effect of other food materials. The use of X-rays in this connection became of interest, not only from the fact that it might reveal something of interest in therapy, but also because it was possible this might prove to be a simple method for testing foods of all kinds.

In the second, third, and fourth series of experiments we tested the addition of lettuce, corn, and carrots to the dog biscuit diet. In several instances we also gave milk, and, in other instances, cod liver oil and cod liver oil and milk. In none of these experiments have we seen sufficient difference to make certain whether one diet is more efficient than the other. Since these experiments are still being carried on, the curves need not be given at the present time.

At the beginning of these experiments it was appreciated that X-ray patients might be greatly benefited by a proper dietary. Such a dietary might protect the organism as a whole against the large doses of X-rays which must be administered in certain cases of cancer. As noted in a previous paper (11) before this Society, the use of dietaries containing green vegetables, small quantities of cream, and cod liver oil has made it possible to prevent many of the systemic effects of X-rays, and also to begin treatment at once on patients with well advanced cachexia. The cachexia has even disappeared in part and the blood picture improved during treatment when such dietaries are used.

We have also used liver in a certain number of these cases. Previous to the work of Minot and Murphy, we (14) had already noted that the secondary anemia of cancer patients disappears by giving ample quantities of green vegetables, cream, and cod liver oil in their diets. While liver may have a specific action, as Minot and Murphy now contend, in the treatment of pernicious anemia, we have so far seen no greater benefit from it than that obtained by the use of cream and cod liver oil. The liver of all animals is a storehouse for the fat-soluble vitamins. The liver of cod fish contains large amounts of them and becomes of commercial importance for this

as well as other reasons. It seems to us that the burden of proof rests with the Boston authors to show that the liver diet is more important than the one we had already outlined at an earlier time (15).

The action of milk in protecting against large doses of X-rays is interesting when compared to the importance of milk in lengthening the life of rats. The white rat in captivity suffers after one and a half to two years from a chronic pulmonary disease, which is associated sooner or later with emaciation and death. Our rats die generally after two years. It has been noted at the Wistar Institute that the feeding of milk cures this pulmonary condition and prolongs greatly the life of the rats.

Our further analysis of the fat-soluble vitamin content of normal tissue indicates clearly that this fat-soluble vitamin content decreases with age. If X-rays act, as these various experiments indicate, to remove the lipoid elements from the tissues, they must produce, therefore, changes in the tissues not unlike those peculiar to age.

STUDIES TO DETERMINE THE EFFECT OF THE RAYS ON CANCER IN TREATMENT

In the treatment of cancer the cancer is not alone treated, but the surrounding tissue is also subjected to the rays. After treatment with X-rays the cancerous tissue does not degenerate at once, but only after a considerable latent period. Burrows (1) (16) (17) has studied the reaction of fragments of cancer and normal tissue in drops of blood plasma in the tissue culture. These studies have shown that the growing cells in these cultures take no measurable nourishment from the plasma itself. In the culture the number of new cells formed is never as great as the original number of cells in the fragment, and for each new cell formed a given amount of cellular material disappears from other cells in the fragment. In the culture the border cells of the fragment migrate from the fragment and grow, while the more central cells degenerate and supply the nourishment for this growth. In studying this degeneration of these cells in the fragment, Burrows noted also that it resembles very much the hyaline and degenerative changes that one sees in the normal tissues about any cancer that grows locally. The spreading cancer causes these same changes to a less degree than those which grow to form a large local mass. The spreading cancers act on a much larger area of tissue, and, consequently, the relative amount of change in any given area is much less than in the large cauliflower growth.

These changes in the tissues also resemble the changes noted about the drops of coal tar and the changes induced by X-rays in the tissues. To prove that they are of the same character it became of interest to study the effect of other actively growing tissues on normal tissues in the organism. It has been known for a long time that hyaline and degenerative changes of this character are peculiar to pre-cancerous lesions (2). It was a question, therefore, whether or not they represented the removal of these lipoid elements of these tissues which are necessary for the primary development of the cancer, and whether the growing cancer cells did not also utilize these same substances for their growth.

A fragment of actively growing embryonic tissue was then injected into the derm of host rats. This tissue grows actively to form often large cystic tumors. This growing tissue produces atrophy, hyaline and degenerative changes in the skin of the host, with the eventual development of atrophic ulcers. When this embryonic tissue is stimulated to grow more actively, true cancerous degenerations are produced in the skin of the host (18).

A study of the growth of fragments of adult, embryonic, and cancerous tissues has

been interesting in this regard. The cells from the cancer fragment begin to grow practically at once when placed in the plasma culture. The growth of these cells is most active for a time, but the whole of these cells always degenerates very early and on account of this early degeneration (which may be as early as 24 to 48 hours), the total amount of growth is never very great. That this early degeneration of the cancer cells is not due to the formation of toxic substances, but, rather, to the lack of nutrition in the culture, can be further shown by the fact that these same cells will grow indefinitely if placed in a plasma to which a minced muscle of an adult animal is added. These same cancer cells can be made to grow for a considerable time if given embryonic extract, but their life is not so readily preserved as when they are fed adult tissues (19).

Similar cells from younger embryos also grow with great vigor in the cultures. These cells, unlike the cancer cells, grow for a much longer time and a considerable bulk of new tissue is formed about such fragments. The cells from a similar fragment of the adult will not grow under these same conditions. They migrate from the fragment after a long latent period, but no growth takes place. As noted above, if they are washed with benzol, plasma, or another lipoid solvent they can be made to grow, and—an interesting fact—the rate and extent of their growth can be varied from that of the cancer fragment to that of the embryo, depending apparently on the amount of the lipoid removed.

An analysis of these various tissues shows that the cancerous tissue contains large quantities of the water-soluble growth-stimulating substances, but no demonstrable lipoid nutrient substances. When these tumors are fed they supply large quantities of Vitamin B, but no Vitamin A. The embryonic tissue contains also large quantities of the water-soluble growth-stimulating substance. When fed, it was found to contain not only large quantities of Vitamin B, but also small quantities of Vitamin A. In the cultures it has been shown that it contains nutrient substances. The adult tissue contains much less Vitamin B and considerable Vitamin A (15).

As is evident, therefore, only those tissues which contain Vitamin A supply food for other cells. The quick death of the cancer tissue *in vitro* is associated with the absence of Vitamin A in the culture medium and cancer tissue. These observations also indicate that those same lipoidal substances which inhibit growth in the body when the tissue is saturated with them, are necessary food constituents for other growing cells.

These lipoid substances are not only necessary for the growth of these cells, but, as other studies have shown, they are also necessary for the function, migration, and other activities of these cells. They inhibit growth when present in excess in the tissue only through the fact that they are insoluble in water and are soluble in proteins and fats. Growth synthesis takes place in a water medium. Proteins and fats saturated with these substances are removed from the water parts of the cell. On the other hand, these same lipoids or substances formed from them are an essential part of the protoplasm of the cell. These lipoid elements which we have grouped under the name of ergusia and which we have shown to be the same or similar to Vitamin A (the fat-soluble vitamins necessary for growth), must act on the cell when present in excess, in the same way as the brake acts on the engine. The brake acts to stop the engine, not through the fact that it has a chemical composition different from the structural parts of the engine. Its composition may be the same. It acts entirely through its form and position.

There seemed to be little doubt, there-

fore, but that the growing cells must find in other cells and tissues certain lipoid substances necessary for their growth. The removal of these substances, as noted above, leads either to growth or to hyaline and other forms of degenerative changes in these tissues. For these growing cells to continue their growth they must be supplied then with tissue rich in these lipoidal substances. When the cancerous tissue is placed in a culture medium free from these substances it dies quickly.

In studying the death of those cancer cells allowed to grow in a medium free from proper nutrient substances, it has been noted that the picture of the destruction is similar to that of the autolysis which results from the lack of oxygen. It differs chemically from autolysis, however, in that no toxic substances are formed. Large cancers degenerating in the body after X-ray treatment also often fail to have any marked toxic effects on the organism. The question arises, then, May not one of the most important factors in the destruction of cancer by X-rays be one of starvation of the cancer cells?

When we commenced our work on the action of X-rays on cancerous and normal tissue we believed that the X-rays killed the growing cells entirely by acting directly upon them. This more careful study and the long latent period between the application of rays and the death of cells suggests that other factors may have also entered in. When we removed the nourishment from the cancer cells *in vitro* they degenerated quickly. The cancer cells in the body obtain their nourishment from the surrounding normal tissues, and these tissues supply nourishment only in proportion to their content of lipoid substance. The X-rays act to remove this lipoid from these tissues. X-rays applied to the cancer and its immediate surrounding tissue must remove the lipoid substances not only from the cancerous tissues, but also from the surrounding tissue, and the cancer cells should die from the lack of nourishment in the time that they are known to die after radiation.

CONCLUSIONS

In this paper we have given the evidence to date showing that one of the actions of X-rays on the tissues is to remove their normal lipoid content. It has been shown also that one of the chief actions of X-rays in destroying cancer may be the removal of these lipoids, not only from the cancerous tissues, but also from the normal tissues immediately adjacent to them. These lipoids are necessary substances for the growth of the cancer cells. Without them, the cancers degenerate quickly.

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THE CANCER CELL IN THE PRACTICE OF MEDICINE[1]

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GENERAL practitioners and specialists who have relied on textbook signs and symptoms for the diagnosis of cancer are becoming aware of the fact that small cancers do not always present differential signs and symptoms; and operative surgeons and radiologists who have gone the limit of radical therapeutic technic realize that this limit is not radical enough to prevent recurrence in many instances.

The universal truth of these statements is supported by the impression derived from the last International Conference for the Control of Cancer (1926): the earlier the diagnosis and the smaller the cancer, the better the therapeutic, curative, and palliative results; the less the necessary therapeutic destruction and hence the less the immediate and ultimate mortality. This message, which has been and must continue to be carried to the lay public and the profession, makes it clear that early diagnosis is still the best key to unlock the cancer problem. It has been spread widely by the American Society for the Control of Cancer and the American College of Surgeons, and it has already borne fruit. By actual measurement, the average size of cancers is less when we see them than it was ten years ago; and the pre-therapeutic differential diagnosis is more difficult without the clinical procedure of biopsy or surgical exploration.

Time will not permit me to review all of the accepted clinical differential diagnostic signs and symptoms. Those given in textbooks are becoming less and less valuable for early diagnosis as one learns from exploration of such conditions as chronic gastric ulcers, intermenstrual and post-climacteric bleeding uteri, nodular breasts, hard adenomatous thyroids, bleeding and partially or periodically obstructed intestines, and small central and peripheral tumors of bones.

In the stomach, intestines, and bones the roentgen ray is perhaps the most valuable of all purely clinical diagnostic instruments because it determines the site of small lesions before differential signs and symptoms appear. This instrument, like all others, has its limitations: there are cancers too small to be recognized as such by its means, although a small pathologic lesion may be seen. This group of small cancers is increasing because the public has been taught to bring its sores and lumps to us before they become too large for successful treatment. Doubtful lesions demand the aid of another type of diagnostic specialist in clinical practice. Until recently, gross appearance, histologic patterns, and the structural status of the basement membrane constituted the only criteria on which diagnostic and prognostic judgment might be founded by pathologists. In practice these have served well in what is now recognized as advanced disease; they are insufficient for the smaller lesions now seen and as one recognizes the necessity of early diagnosis and early radical treatment. One looks now for every possible method by which cancer may be recognized before it reaches the stage of gross and even histologic recognition. The smallest cancerous ulcer of the stomach in this series is 1 cm. in diameter and the smallest with glandular involvement is 1.2 cm. in diameter. These facts make it important to discover the stages before the lymphatics of the stroma are invaded.

For the last twenty-one years I have sought criteria of earlier microscopic di-

[1]Read before the Radiological Society of North America, at New Orleans, Louisiana, November 29, 1927.

agnosis than have been used by histopathologists. Beginning in 1912 I described three cytologic conditions associated with chronic irritation in the mammary acinus, the gastric tubule, the prostatic acinus, and the skin. The suspicious condition was called secondary cytoplasia (Figs. 1 to 6). It was seen clearly that in these chronic conditions there was sometimes a cytologic change characterized by replacement of adult and reparative regenerative cells by undifferentiated cells resembling morphologically the malignant cells which had been found in specimens known to be cancer. At no time in the studies was secondary cytoplasia ever called cancer. I do not know now that such an early stage would kill the patient were it actually cancer. I am merely presenting the facts which show clearly a cytologic analogy between that which has been called cancer and something which has apparently not been seen and regarded as such by histopathologists.

The malignant or cancer cell has certain definite characteristics: it is ovoidal or spheroidal; it has a relatively larger nucleus than any adult tissue cell; in the nucleus one finds one or more large nucleoli which by actual measurement have a greater average volume relative to the volume of the nucleus than the nucleoli of reparative regenerative cells any place in the body; the cytoplasm of the malignant cell is less dense than that of either the adult or reparative regenerative cell; the nucleoplasm is more granular and denser than that of the reparative regenerative cell (Figs. 1 to 7). The characteristics as I have just described them cannot be seen in tissues which have been fixed and embedded in either paraffin or celloidin. They can be seen in perfectly fresh unfixed and unstained specimens. They may also be seen in fresh unfixed specimens stained with Unna's polychrome methylene blue or Terry's modification of this stain. Recently Terry has perfected his stain for fixed but

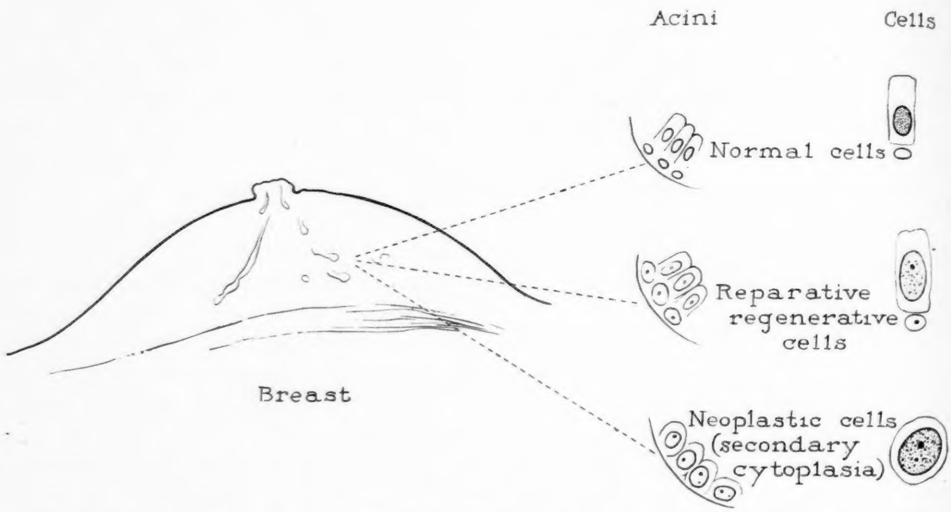

Fig. 1. Breast and its acini showing cytologic changes which are seen frequently in chronic mastitis. Normal and reparative regenerative cells are sometimes replaced by cells having the morphology of malignant cells.

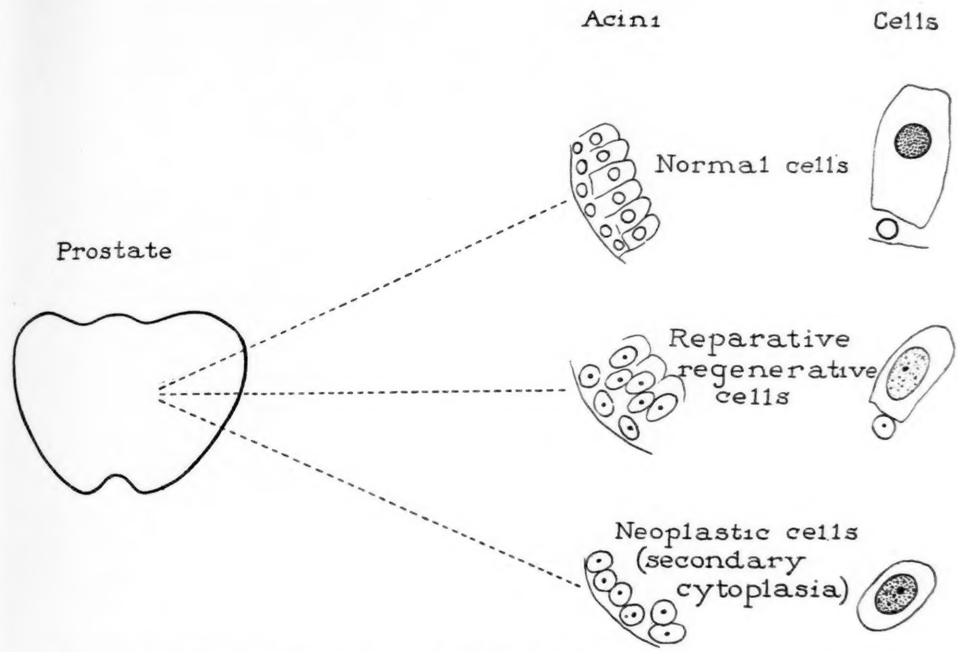

Fig. 2. Prostate and its acini showing cytologic changes which are frequently seen in chronic prostatitis. Normal and reparative regenerative cells are sometimes replaced by cells which have the morphology of malignant cells.

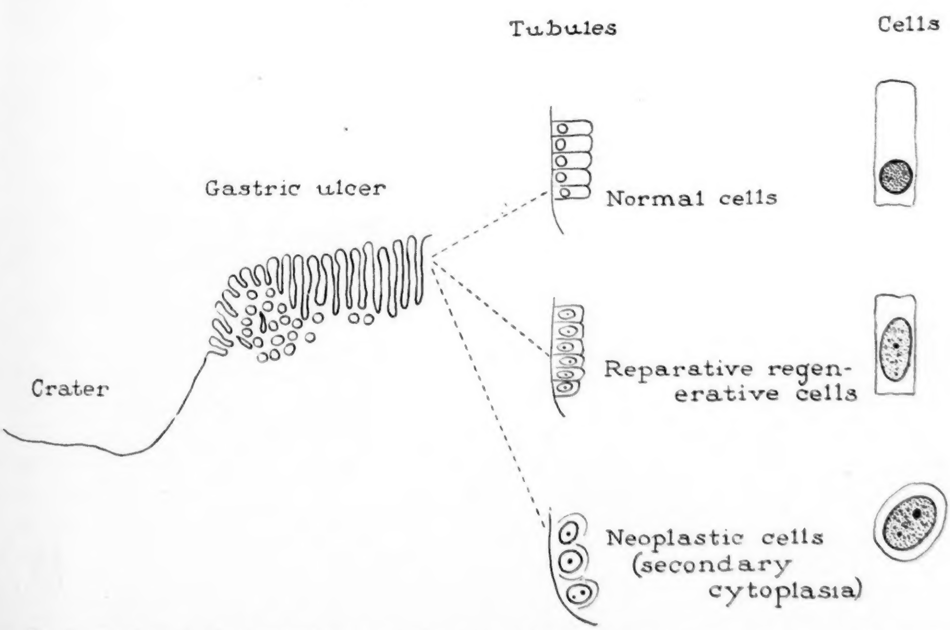

Fig. 3. Border of chronic gastric ulcers some of which show normal cells, some regenerative cells, and some cells which have the morphology of malignant cells.

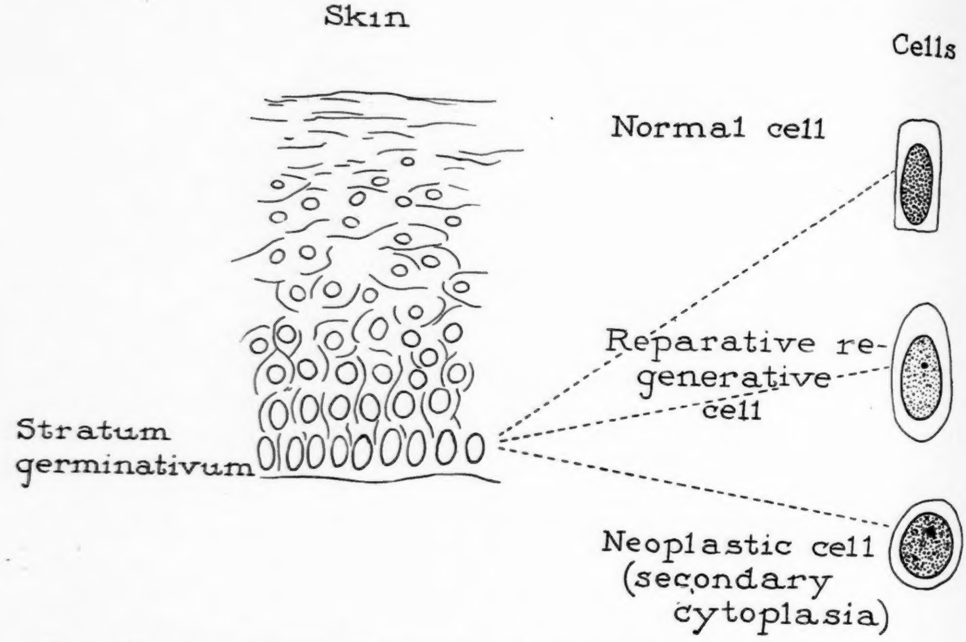

Fig. 4. Skin showing cytologic changes seen in the stratum germinativum in chronic dermatitis. In secondary cytoplasia the cells of the stratum germinativum are replaced by cells morphologically identical with malignant cells despite the fact that they have not invaded the underlying stroma.

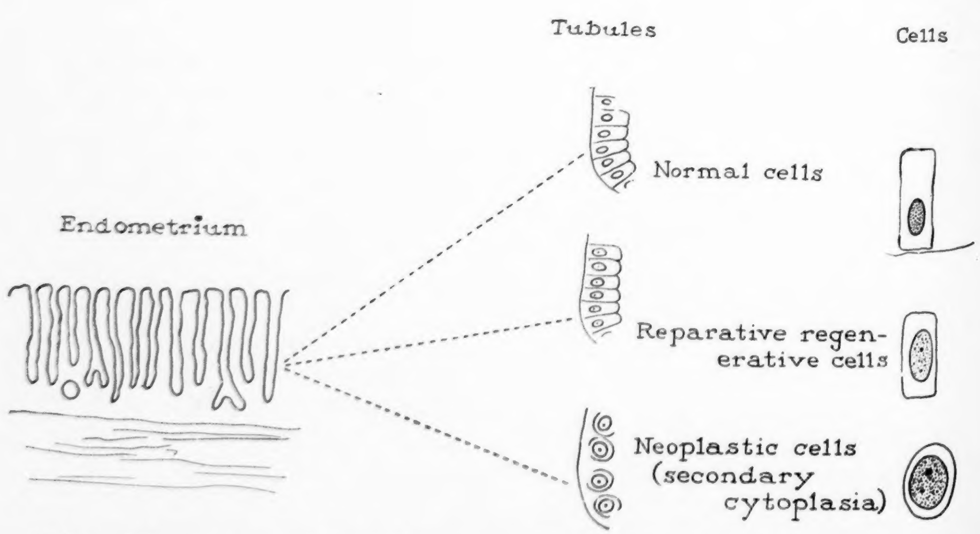

Fig. 5. Endometrium showing cytologic changes seen in uterine tubules. Normal and reparative regenerative cells are sometimes replaced by cells having the morphology of malignant cells.

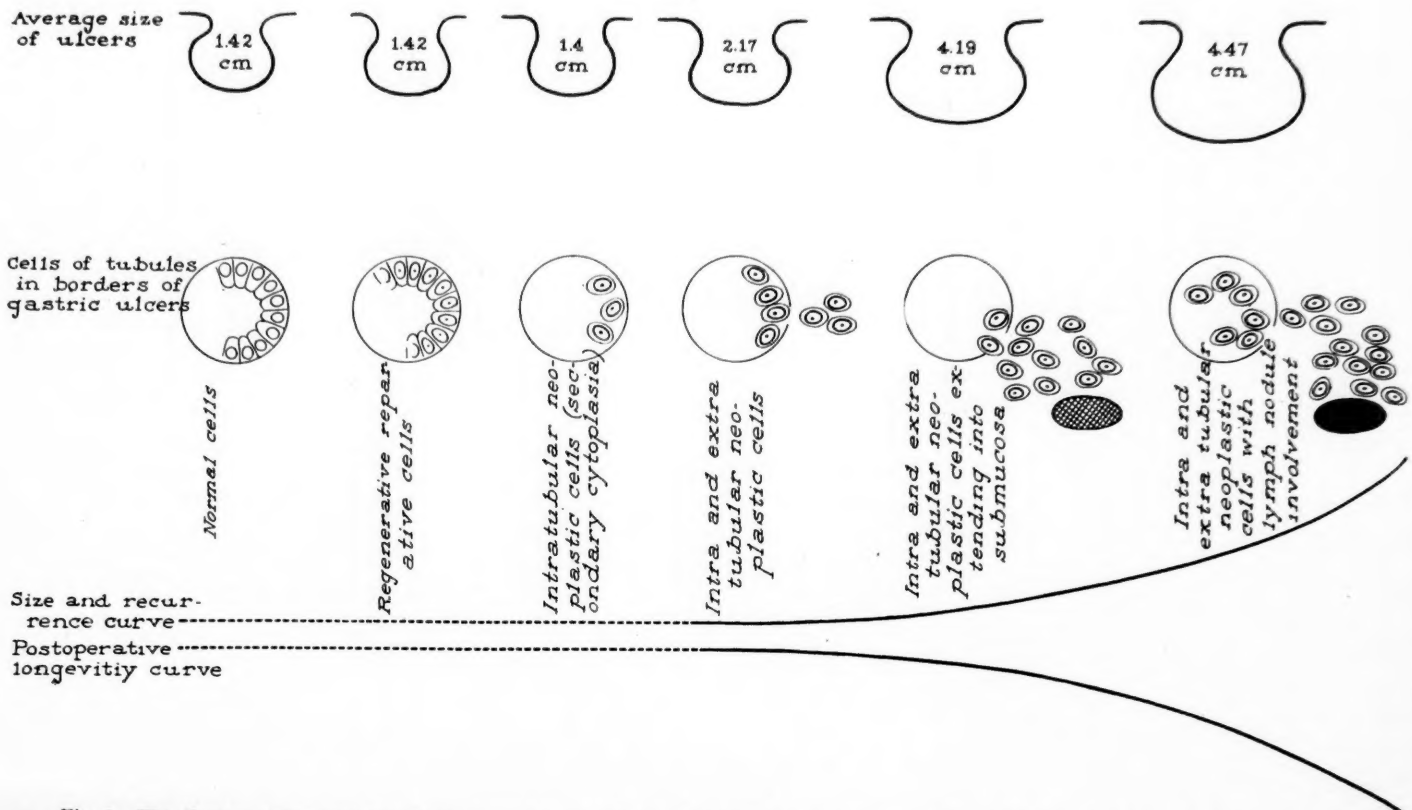

Fig. 6. The diagram shows cytologic changes seen in the tubules of different gastric ulcers. The solid lines indicate the real and the dotted lines the hypothetical behavior curves if the condition described as secondary cytoplasia is an early stage of cancer.

not embedded tissues. One may prepare microscopic specimens with a freezing microtome, by teasing, by the razor method as it was used by older pathologists, or by that recently described by Terry. In the hands of an expert cytologist any of the methods will suffice, but none of the methods is safe unless the observer and interpreter is thoroughly familiar with the high-power mor-

Fig. 7. Typical malignant cell in a fresh unfixed condition. This type of cell is seen outside and inside of tubules and acini in cancer. It is sometimes seen inside tubules and acini alone, a condition which must be looked on with suspicion.

phologic details of every adult cell in the body, those of all reparative regenerative forms and those of various malignant cells, and knows well the degenerative changes which may alter and confuse the picture. There is no specific staining reaction for the malignant cell but there are certain physical criteria by which it may be recognized in most if not all instances. At least one can say that the malignant type of cell differs from all others.

Whenever cancer is present the cell which I have described as analogous to the cancer cell is always seen in the tubules or acini of the organ affected. We know now that it is present sometimes in acini and tubules when there is no visible cancer in the rest of the specimen. Its morphology is so characteristic that a diagnosis of cancer can be made from a single cell in the sinus of an inflammatory lymph node. This has been repeatedly done from lymph nodes in cases of cancer of the stomach and breast, without the cytologist even knowing that he was examining a lymph node from a patient with cancer. There will be some inexperienced observers who will mistake the reparative regenerative cells in tubules or acini and outside of these for the malignant cell. The difference in morphologic details and the relative proportions of nucleolus to nucleus must be carefully learned by experience. In case several cells are present their arrangement in relation to each other is also important. The axes of the nuclei of intratubular and intra-acinic reparative regenerative cells are usually parallel or approach parallel, while those of true malignant cells bear no constant relation to each other (Figs. 1 to 6).

It must be clearly understood that, despite the fact that I have been working with this cell for many years, I have never called it cancer when inside of the acinus or tubule At no time has a radical operation been advised for this condition, but, as one proceeds in experience and studies the results of treatment, one finds that even the smallest cancers are sometimes associated with lymph-nodal involvement. We must, therefore, begin to attack radically all conditions which show any analogy to cancer, especially when that analogy has to do with the actual living unit of such a disastrous disease. In my opinion, it is no longer efficient to wait and attempt to pin a textbook name on a neoplastic condition before dealing with it therapeutically. In most instances if we wait for the typical histologic criteria which justify our different classifications, we will have waited until it is too late. The only important practical procedure with our present

knowledge is to determine whether a cytologic condition is dangerous or not.

In a recent review of 1,683 resected or excised gastric specimens for chronic ulcer and for cancer, there are some very suggestive facts. The records were made as a routine over a period of eleven years. The specimens were studied from the standpoint of relation of the size of ulceration to the amount of malignant involvement. Thus in this series it was found that the average diameter of cancer of the stomach with lymph-nodal involvement (516 specimens) was 4.47 cm.; that without lymph-nodal involvement (298 specimens) it was 4.19 cm. During the making of diagnoses and records it was occasionally necessary to call some "early carcinoma," by which is implied the presence of secondary cytoplasia and a few malignant cells in the stroma of the mucosa. There were forty-six such instances and all were chronic ulcers. The average diameter of these early cancerous ulcers was 2.17 cm. There were thirty-nine ulcers in which only secondary cytoplasia was present; the average diameter was 1.4 cm. During this same period 784 simple chronic ulcers were excised or resected for diagnostic as well as therapeutic purposes. It was impossible to be certain clinically that cancer was not present. The average diameter for the simple ulcers was 1.42 cm. If secondary cytoplasia is the immediate pre-cancerous condition or even cancer in its early stages, then it would be natural to find it in simple chronic ulcers when they are still under the average diameter of 2.17 cm. This series of facts adds weight to the observation which I made many years ago that practically every chronic gastric ulcer over 2.5 cm. in diameter was found to be malignant. During the same period 2,267 specimens of cancer of the breast and of chronic mastitis with secondary cytoplasia were studied as to size of the involved portion. The average diameter of mammary cancer with lymph-nodal involvement was 2.35 cm. and without lymph-nodal involvement, 2.13 cm. There were twenty-one cancers less than 1 cm. in diameter with no lymph-nodal involvement and five less than 1 cm. with lymph-nodal involvement. As in the study of cancer of the stomach, certain specimens were called "early carcinoma." There were eleven such specimens and the area of chronic mastitis containing the cancer had an average diameter of 1.7 cm. The areas in chronic mastitis designated as showing secondary cytoplasia (seventeen specimens) had an average diameter of 0.92 cm. The smallest typical cancer of the breast I have seen was less than 2 mm. in diameter. There is a suggestive sequence in both series, especially so since in 12.5 per cent of the cases of "early carcinoma" of the stomach the patient died of recurrence within the period of eleven years. None of the patients suffering from secondary cytoplasia in the stomach is known to have died of cancer, but 7.5 per cent are known to be dead of unknown cause. None of the patients suffering from "early carcinoma" and secondary cytoplasia in the breast has died of recurrence so far as can be determined.

That every early or small cancer must necessarily kill the patient, with or without treatment, cannot be demonstrated, but that we have no means of telling which will not is very certain. We have no means of telling which patient with tuberculosis, diphtheria, typhoid fever, small-pox and many other diseases in early stages is going to die. In fact, some do not die but all must be treated with the idea that they might die if not well cared for by the methods best approved. There is much evidence that the human body does attempt defense against cancer, even in those instances when the defense is not successful. The following table gives some suggestive figures in fatal cases of cancer in various regions.

	Stomach 99 cases, years	Breast 92 cases, years	Rectum 102 cases, years	Skin 29 cases, days
Average length of post-operative life with lymphocytic infiltration	2.73	2.51	1.57	496.2
Average length of post-operative life without lymphocytic infiltration	2.7	2.48	1.31	346.6
Average length of post-operative life with fibrosis	....	2.72	1.53	655.7
Average length of post-operative life without fibrosis	....	1.87	1.29	295.6
Average length of post-operative life with hyalinization	....	2.81	2.33	449.6
Average length of post-operative life without hyalinization	....	2.21	1.44	437.9

The various combinations of these factors are associated with even greater increase of post-operative longevity, which is seen at its best when all factors together are checked against their complete absence. The following table shows this.

	Breast 92 cases, years	Rectum 102 cases, years	Skin 29 cases, days
Average length of post-operative life with lymphocytic infiltration, differentiation, fibrosis and hyalinization	4.4	2.25	444.6
Average length of post-operative life without lymphocytic infiltration, differentiation, fibrosis and hyalinization	1.52	0.76	54.0

These factors are present frequently in secondary cytoplasia and even during reparative regeneration, thereby suggesting that the body itself reacts in a defensive manner against the possibility of invasion by the cell which has the physical characteristics of the cancer cell.

The malignant cell, which is itself a parasite, has just as definite a place in the practice of medicine as the bacillus of tuberculosis or the *Spirochaeta pallida;* and, whenever any practitioner is dealing with any chronic local ulceration or tumefaction, its presence must be ruled out if the disease does not become healed or disappear in a few weeks. This is especially true in the absence of foreign bodies, tuberculosis, syphilis, actinomycosis, blastomycosis, and perhaps some rare skin diseases. The affected area or mass should be excised if possible for diagnostic purposes. If the malignant cell is in the stroma, a radical operation with regional lymphadenectomy should be performed, provided the immediate operative risk is not too great. If the characteristic cell is found only in the tubules or acini and not in the stroma, then wide local removal is the only necessary procedure with our present knowledge. All such cases should be followed, however, for the possibility of recurrence.

Despite the fact that, according to the old criteria, we have no right to call this cancer, the more we see of small cancers and their behavior the more I believe we will soon be compelled to require a radical and complete operation for even the condition of secondary cytoplasia. Since the condition can be recognized only in fresh tissue, the diagnosis should be made at the time of exploration or biopsy.

It is by such methods of early diagnosis that we shall be able to meet successfully the public demand for early treatment which we, as a profession, have publicly advised.

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CANCER BIOLOGY AND RADIATION[1]

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NOT very rapid progress has been made in recent years in our knowledge of the more intimate biological qualities of human tumors. The studies of MacCarty, Broders, Martzloff, Greenough, and others, especially of the French school, have shown, however, that a beginning has been made toward an understanding of the biology of human tumors, based upon an analysis of their histology, but the facts are few as yet. Some knowledge also has come from careful clinical study.

The greater control over the conditions of investigating animal tumors possessed by the experimentalist has led to much more accurate knowledge than is possible in clinical study. Foremost, perhaps, in general interest are the recent discoveries of Warburg on the conditions of the breaking down of glucose in the body cells. As you know, he found that normal tissues used glucose by oxidizing it in the presence of oxygen into carbon dioxide and water, while tumor cells are capable of splitting large quantities of glucose in another direction, that is, breaking it up anaërobically into lactic acid. The Coris demonstrated that there was a larger amount of lactic acid in the blood leaving a fowl tumor than in that entering it, and this has been confirmed on the human subject. For a time it was supposed that this was a long sought characteristic difference between tumor cells and normal cells, but it was shortly found that retinal epithelium, leukocytes, embryonic structures, and placental tissue were all capable of splitting glucose in the absence of oxygen into lactic acid. Thus anaërobic glycolysis is not a characteristic of the tumor cell nor does it explain why the normal cell becomes a tumor cell, though Warburg has revived the old hypothesis (See, for example, Wyss, *München. med. Wchnschr.*, 1907, LIV, 1576) that when normal cells are subjected for a long time to partial oxygen starvation they may in some way adapt their metabolism from the oxidation type to the lactic acid type and thus become cancer cells. But if this were true, then the tissues of the embryo, placenta, bone marrow, and the retina should act as tumors. Perhaps this special type of glycolysis is only an expression of one of the capacities of rapidly growing cells. It is difficult to obtain rapidly growing normal connective tissue of the adult type in sufficient quantities to study, so that we cannot be sure, for instance, that the connective tissue cells of granulation tissue would not be capable of the same type of metabolism as the tumor cells. Further investigation must be carried on along this line in order to furnish more knowledge before any important conclusions can be drawn.

It has been reported that if animals are kept in an atmosphere low in oxygen the tumors will disappear, but these, after all, are grafted tumors. They are not in the medium in which they originally developed, and, as has long been known, spontaneous disappearance is not infrequent in tumors of various types, necessitating the most careful repetition of such experiments on a large scale. It was immediately thought that the administration of insulin might reduce the growth-activity of tumor cells. While such an observation has been reported by certain workers, it is not clear that sufficient care was taken to avoid confusion with spontaneous disappearance. Such experiments should always be carried on with tumors that do not spontaneously disappear or, if possible, with primary tumors.

The same is true of the attempt made

[1]Presented before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 28–Dec. 2, 1927.

some years ago to cure tumors by the administration of large doses of phloridzin, a substance which makes the kidneys permeable to sugar, and thus removes from the body all surplus glucose. But in an investigation of the subject by McLean and myself, published some years ago, it was shown that this was not a fact, and that the disappearance of the tumors was probably due to other conditions, the growth used being a sarcoma which undergoes spontaneous recession in a high percentage. Certain criticisms of our work were made by the original investigators, so a repetition of the experiment on a considerable scale with various preparations of phloridzin was again carried out by Dr. Morris in my laboratory. His results confirmed the original ones by McLean and myself, and showed that the removal of all possible glucose from the organism did not cause a disappearance of the tumors. The study of advanced diabetics in whom all surplus sugar is excreted has also shown that the mere removal of sugar from the system does not prevent the tumor from getting glucose enough to keep on with its growth. Of interest in this connection is the disappearance of the glycosuria and the symptoms of diabetes as the neoplasm enters the terminal phase. This change has been attributed to the great sugar-splitting powers of the tumor cells, but as the phenomenon appears only in the late stages of the neoplastic condition, partial starvation due to weakness and lack of appetite probably plays a part.

The other aspect of the question, that is, the stimulation of tumor-growth by the administration of glucose, has been tried by several Austrian radiologists, who believe that by stimulating the tumor to increased activity better effects are obtained from radiation. They overlooked the possibility that metastases out of range of the radiation might also be stimulated. But Prime was unable to demonstrate this in animal tumors. He showed that if in rats an inoculated tumor is allowed to reach a certain size, and then the animal given large intravenous injections of glucose, the amount of X-ray required to kill all cells of the tumor receiving such injections showed no essential difference from the amount required to kill the tumors in animals not receiving such increased doses, and further investigations of the clinical results have not rendered it probable that the effects originally observed were anything but accidental. No effect should really be expected, for the blood of most diabetics contains a large excess of free glucose and no excessive virulence or growth-rapidity is found in cancer arising in the course of that disease.

The courageous attempt of Gye and Barnard to rehabilitate the old idea of the causal relation between bacteria and tumor-growth has apparently been a useless gesture. Gye's demonstration of what he supposed to be a combination of a virus and a chemical adjuvant, the combination of which produced tumors, has not been reproducible in other laboratories, and the demonstrations by Carrel and others that filterable tumors could be obtained in the fowl by tar and other reagents has rendered the presence of a living virus questionable. Rather, it seems as if the Rous tumor were due to some chemical substance which acts as a stimulant to the tissues of the fowl, and that in the mammalian tumors the situation is quite different. A repetition on a considerable scale of the older filtration experiments on a series of rat and mouse tumors has almost universally led to negative results. The same is true of a rabbit tumor.

The report of Sittenfield on positive results of such transmission by filtration points only to the necessity of extremely careful technic, for his statements have not been confirmed by others and the fact that fragments of tumor cells can get through the

pores of filters highly impermeable to bacteria renders it possible that all positive results hitherto obtained have been due to the escape of viable cell particles of minute size rather than a demonstration of the presence of a true filterable virus. No information exists, for instance, concerning the smallest fraction of a mammalian cell from which regeneration can take place. Possibly under favorable conditions individual chromosomes, or even fragments thereof, might suffice.

The whole question is surrounded by great difficulties in technic and until some better methods of demonstrating ultramicroscopic organisms are made available by the bacteriologists the demonstration of an ultramicroscopic cause of cancer remains in a precarious state.

A large amount of work has been done recently on the subject of the action of radiation on tumors. The morphological changes which accompany the destruction of tumor cells by X-ray and γ-rays have been shown by myself and others not to be characteristic of these radiations, but an effect common with other physical agents, such as heat and cold, on the cell. The facts have been summarized by Alberti and Politzer.[2] The experiments from different laboratories have covered such various materials as tumor cells, the eggs of *Ascaris*, plant cells, corneal epithelium of the salamander, and embryos of various lower animals. Chemicals and ultra-violet light have been shown to have similar effects upon the nuclei of the cells. It is, therefore, probable that any physical agent, within limits, will cause the same sort of chromosomal changes as the limited region of radiation comprised in X-ray and radium radiation.

The laws governing the destruction of the cells by radiation have been shown, largely by work in the Crocker Laboratory, to be the same as those governing the hemolysis of red cells, destruction of bacteria by disinfectants, and the death of a standard human population. The curves when plotted on Cartesian co-ordinants have an S-shape. They do not form a straight line on logarithmic plotting as was thought by Chick and Arrhenius from their studies on hemolysis. On logarithmic probability paper they plot fairly well in a straight line, the slope varying with the different biological materials, but even in this case there may be aberrations if the initial and terminal stages are included. No analytical expression has as yet been found to cover the observed data, and it is probable that while a formula could be fitted by the methods devised by Karl Pearson, such laborious arithmetic computations would furnish nothing of value in the interpretation of the underlying principles. The fact is that a continuous destructive agency, acting upon a population of highly variable sensitivity, causes the death of cells in so irregular a manner and possibly by such different modes that all we can do is to find that the curves for a given material are reproducible. My own original experiments, begun in 1913, with radium and X-ray on animal tumors, already discussed before this Society, have been found to furnish a group of curves very similar to each other, varying solely in the quantity of radiation required to destroy a given percentage of the cells. Some tumors require double the amount of radiation to kill all the cells that is required to kill 50 per cent. Some require more and other tumors somewhat less; while with the eggs of the *Drosophila* Packard has shown that to kill all the eggs requires some three times as much radiation as that for 50 per cent. This merely means that the tumor material is in general more nearly homogeneous as regards its sensitivity than are the *Drosophila* eggs. Probably the same condition applies to human tumors with cells of greatly vary-

[2]Alberti and Politzer: Archiv für mikroskopische Anatomie, 1924, C, 83.

ing differentiation. For example, the slow-growing squamous cell epitheliomata may have tumor cells in the rapidly growing portions that are fairly susceptible, while those which have undergone cornification and are in a quiescent phase must be much more resistant. The study of sections of heavily rayed human material would seem to show this. The only way in which it could be actually demonstrated would be by the exposure of tissue cultures in various stages of development, but up to the present it has been extremely difficult to grow even most actively proliferating human tumors.

As a corollary to these experiments it has been found that for particles of small size, such as tumor cells, *Ascaris* eggs, or the eggs of the fruit fly, the destructive effect is independent of the wave length, provided the measurement of the radiation intensities is made with an open ionization chamber of the Duane type. It seems probable, though not proved, that the erythema dose on the human skin will obey approximately the same law where full allowance is made for complicating factors.

Definite proof of the wave length factor has not yet been obtained for gamma rays of extremely short wave length, owing to the difficulty of accurate quantitative measurement of these rays, nor has proof included the recently introduced long radiations which have but little penetrating power. It is not always understood by those who discuss the subject that differences in biological effects may be expected between those rays which affect the tissues primarily through the medium of atomic discharges and those which act on molecular complexes, so that, therefore, the laws for very short wave lengths may not apply to the damage produced by heat or ultra-violet light, which presumably act in a different way. Comparative measurements of the energy absorbed in the tissue cells from heat rays, ultra-violet light rays, and X-rays have not yet been made with sufficient accuracy to settle the question.

An interesting confirmation of these wave length studies on biological materials has been recently obtained by Glasser and Fricke, using hemoglobin solutions.

The ease of reading and cheapness of the *Drosophila* material has rendered possible not only the standardization of X-ray machines for clinical uses, but has confirmed with surprising ease many of the laboriously obtained facts concerning radiation. The increase in surface dose from back-scatter with large portals and short wave length X-ray, depth dosage with different portals and wave lengths, etc., all are easily demonstrable. The material is very constant and obtainable in every part of the world. The technic of manipulation is easy, and the results can be read in forty-eight hours, so that it is to be hoped that larger use may be made of this very simple means of estimating biological dosage.

The experimental study of the action of other agents on the cell has received a considerable impulse from the investigations of Blair Bell on colloidal lead. The demonstration of the mode of action is complicated by a number of factors, one being the purely mechanical necrosis determined by vascular thrombosis induced by the suspensoid itself. We have been able to demonstrate this thrombosis with wholly inert colloidal material, but the lead apparently has also a direct toxic effect on the cells, which explains why colloidal lead is effective in the destruction of tumor cells experimentally, while colloidal gold has but little action. In other words, the lead in the tissues acts, as Blair Bell has experimentally shown, directly on the cell, while inert substances like sulphur, carbon, some of the colloidal dyes, and colloidal gold have no such secondary action. That the secondary radiations from the trace of the metal in the tumor play any part in such destruction when the tumor is radiated with X-ray has been shown by

Holthusen and others to be more than doubtful. The amount of such metal present is much too small to explain the results, and my own experiments have shown that with certain tumors a distinctly beneficial effect amounting to some 20 per cent has been obtained by administering lead and then radiating the tumor. This has not been found with certain other colloids and, therefore, the special lead action must be due not to the secondary rays but to a real toxic effect on the tumor cells themselves, just as was shown in my laboratory some years ago, by Rohdenburg and Prime, that the combination of heat and X-ray was slightly more effective than either agent alone.

For twenty-five years the attempt has been made to treat tumors by sera and vaccines. Jensen was the first to make an anti-tumor serum and claim results. But he soon acknowledged that his cures were due to the hitherto unrecognized process of spontaneous disappearance of the grafted tumors. Recently Lumsden has repeated the work, obtaining what he believes to be an anti-tumor serum, by injecting rabbits with rat tumor material. If the tumor is grafted in the animal's leg and the circulation constricted for a time, mechanically or by the injection of adrenalin, cures can be obtained, but if the serum is exhibited intravenously, no such happy result occurs. The organs of the body absorb the anti-serum as rapidly as the tumor. Many think that Lumsden's serum is not anti-tumor but only anti-rat. Attempts have been repeatedly made to immunize the human body against a growing tumor by injection of killed tumor cells, but all have failed. This result might have been expected from animal experiments in this same line, which also regularly failed to show any immunization to growing tumors. Fibiger has recently shown that the injection of non-specific substances, such as embryo skin, prevented, to some extent, metastasis formation though the primary tumor was uninfluenced. This work was done on tar tumors in mice. Thus no immunity of the bacterial type can be obtained by injection of tumor materials into animals of the same species and no antibodies are demonstrable in the serum of animals so treated.

Certain experiments indicate that the immunity to transplanted tumors is a cellular one, not humoral. Possibly the reticulo-endothelial apparatus is responsible. Homologous skin grafting is possible if this system is blocked by trypan blue, but such blocking does not improve the percentage of positive tumor grafts in partially immune animals, nor does it present spontaneous recession.

It is possible that the various attempts at immunization have been too ambitious. They may have some effect which is masked by the high virulence of the animal tumor, just as colloidal lead has been found to have some effect on the slow-growing, less malignant neoplasms, but not on the rapidly growing, very malignant animal tumors. It seems to me that a useful future field for investigation lies in trying combinations of various sorts. For example, lead plus some anti-human serum. Perhaps the lead may affect some portion of the cell, while a serum would affect another, and when X-ray to the limit is added a certain number of tumors may be affected favorably.

Unfortunately as we approach a complete knowledge of the physical aspects of radiation and the technic becomes more and more perfect, we are faced with problems still more difficult than any previous one. These are, how to apply a sufficient dosage without damaging the patient and yet kill the tumor, and also how to tell what tumor will yield to radiation and what will not. Some insight into these questions must be given before radiotherapy becomes a scientific method.

THE DIRECT AND INDIRECT ACTION OF RADIATION ON CANCER TISSUES[1]

By A. LACASSAGNE, Assistant Director of the Pasteur Laboratory of the Radium Institute, PARIS

THE problem of the mechanism of action of radiations (X-rays and radioactive substances) on the vital elements assumes a truly imperious character with regard to pathologic and especially malignant tissues, because it commands the orientation of our therapeutic measures. At the present time, in spite of the fact that this question is far from settled, the technics employed by the different schools of radiotherapy vary as they favor one or the other solution of the problem.

The essence of this problem is well known. To explain the destruction of cells by radiation one may admit—

1. *A Direct Action.* — The radiations provoke in the cell itself, within the molecular structure of which its living matter is composed, a disruption of equilibrium, which results in the more or less rapid death of the element itself or of its derivatives.

2. *An Indirect Local Action.*—The rays irritate the general tissues which supply nourishment, and the death of the cancer cells is the result of the increase in the local defensive processes: phagocytosis, changes in circulation, sclerosis, etc.

3. *An Indirect General Action.*—The radiations liberate into the circulation, from the tissues, a substance which acts either as a toxin on certain cells, or as a stimulant to certain general organic reactions.

One may think that the solution of this question will come from progress in biologic physical chemistry. Numerous researches have already been carried out along these lines, but none of them has succeeded in giving a satisfactory explanation of the changes seen in certain cells after irradiation. Thus, in the development of my subject I shall consider the problem only from the points of view of experimental histology and of clinical observation.

The discussion of this mechanism of action of radiation has already led to innumerable publications. I believe it is permissible to say that agreement is not far from being established concerning the normal elements; the radiations exercise *directly* their elective cellular effects, and the indirect effect, even by those authors who admit such an effect, is no longer considered as an accessory phenomenon. Only recently Jolly and Lacassagne (21), Jolly and Ferroux (20), Lacassagne and Gricouroff (26), Ferroux, Gayet, and Jolly (11) have brought fresh evidence to confirm this long-established opinion.

The situation is quite different concerning pathologic tissues. The problem is rendered much more complex because of the obscurity with which it has been surrounded by the ill-understood factors of the morbid process under consideration. I shall not touch upon the very different question of the action of radiation on infectious diseases, and I shall limit myself strictly to a consideration of cancerous tissues.

EXPERIMENTAL FACTS ADDUCED IN SUPPORT OF THE INDIRECT ACTION OF RADIATION ON CANCER

Many authors have tried to give an experimental basis to the still much debated hypothesis of the defense of the organism against cancer, and they believe they have demonstrated, at the same time, the indirect action of radiation. From the beginning of

[1]Read before the Thirteenth Annual Meeting of the Radiological Society of North America, at New Orleans, Nov. 28, 1927.

radiotherapy two opposite opinions have been held. Apolant (1) concluded from his experiments on irradiation of cancer grafts in mice that there is direct and elective action on the cell. Bashford, Murray, and Cramer (4), on the contrary, admit that the death of the neoplastic elements is the result of the subdivision, the anemia, and the compression to which they are subjected by the proliferation of connective tissue.

After these last authors, who initiated the indirect local theory, others saw in the lymphocytes the immunizing agents which radiations either excite or inhibit; still others admit a humoral theory, but hold that the radiations liberate into the circulation a substance analogous to a hormone capable of increasing the resistance to cancer.

I shall review briefly the most important experiments on which these hypotheses are founded, and the objections which have been opposed to them:

1. The fundamental fact which has served as a basis for most of the subsequent experiments was brought forth by Bashford, Murray, and Cramer (5): *an animal from which a tumor has disappeared after irradiation acquires an immunity against another graft of this tumor.* Contamin (10) confirmed the fact that a piece of tumor irradiated *in vitro* and inoculated into animals is absorbed, and that the animal thus inoculated has become refractory to a subsequent inoculation. This fact, admitted by many experimenters, notably Wedd, Morson and Russ (52), Lepper (28), Mottram and Russ (31), has been contested by Wood and Prigosen (55), whose investigations bore on several thousand animals.

However, this fact has been interpreted in different ways. While, according to Contamin (10), the tumor cells have been killed by the direct action of irradiation before their inoculation, Chambers and Russ (7) believe that, in irradiated tumors, the malignant elements may still be viable at the moment of transplantation and may die only after they are in the new host.

2. *General irradiation with strong doses destroys the natural immunity to cancer grafts.* According to Murphy (32), fragments of rat cancer grafted into mice are tolerated for a longer time if the mice have been irradiated previously. Chambers, Scott, and Russ (8) think that by irradiation they have facilitated the grafting from rat to rat of a spontaneous epithelioma (the first passage was successful in only one of seven animals). Wood (53), however, was unable to reproduce Murphy's experiment. Moreover, he was unable, by preliminary irradiation, to increase the receptivity of guinea pigs to a sarcoma difficult to transplant. The experiments of Prime (41), conducted with a strain of mice furnishing a large number of spontaneous cancers, yielded the same negative result. I have tried in vain to obtain a take, in irradiated rabbits, of grafts from metastastic lesions of very malignant cancers induced in rabbits by means of tar.

3. *General irradiation with strong doses destroys the acquired immunity against cancer grafts.* Murphy and Morton (35), Mottram and Russ (31), Russ, Chambers, and Scott (42) obtained such a result, whereas neither Sittenfield (46, 47) nor Prime (40) was able to modify, by irradiation, the natural or acquired immunity to cancer.

4. *General irradiation with small doses produces immunity against cancer grafts.* This experiment was first done by Frankl and Kimball (16) by means of transplantable tumors. Murphy and Morton (36) extirpated their tumor from mice with spontaneous cancers, then irradiated the animal, which ceased to be receptive to its own tumor. Russ, Chambers, Scott, and Mottram (42, 43) and Caspari (6) succeeded in immunizing against cancer grafts by general irradiation with small doses. But Fraenkel

and Fuerer (15), Sittenfield (46, 47), Prime (41), and Sugiura (51) obtained, in animals irradiated, a percentage of takes as large as in the controls.

5. *The general irradiation of an animal bearing a cancer graft will produce regression of the tumor even when the latter has been protected from the rays.* This experiment, first done by Russ, Chambers, and Scott (42), was repeated with success by Kok and Vorleander (25), but, on the contrary, gave no result in the hands of Wood (54).

6. *The inoculation of cancerous tissue treated by lethal radiation not only gives immunity but produces retrogression of tumors already developed.* Chambers, Scott, and Russ (9) admit such an action, which is contradicted by the experiments of Wood and Prigosen (55) and of Small, Evans and Krumbhaar (49).

7. *Preliminary irradiation of the implantation area of the graft prevents it from taking.* Frankl and Kimball (16), Murphy, Hussey, Nakahara, and Sturm (33), Murphy, Maisin, and Sturm (34), Kok and Vorlaender (25), and Russ and Scott (44) obtained this result, even with doses much lower than those which, when administered to the tumor before grafting, did not hinder it from taking. On the contrary, Fraenkel and Fuerer (15) and Lacassagne and Samssonow (27) did not succeed, by local irradiation, no matter what radiologic technic was used, in preventing the graft from taking.

8. *A tumor subjected to strong irradiation* in vivo *and transplanted immediately afterward is likely to develop; whereas a tumor irradiated with the same dose and transplanted some days after irradiation is likely to be absorbed.* These experiments of Keysser (24) were repeated recently by Mottram (30). Wood (54) has attempted to explain such a result: according to him, the lesions produced in the cells transplanted immediately after irradiation have not yet become manifest; on the contrary, the graft will take a few days later, at the time of maximum damage to the cells, and then these cells will not be able to withstand the shock of the fresh traumatism incident to the transplantation.

9. *The cellular alterations in irradiated cancers, which have been described, can be found in unirradiated grafts which regress after transplantation into a soil previously irradiated.* To this argument, advanced by Nakahara (37), Wood (54) has forcefully objected that the cellular alterations from radiation have not a specific character and that it is not surprising that similar changes may be seen in a graft in process of absorption.

GENERAL CRITIQUE OF THE PRECEDING EXPERIMENTS

Among all the experiments which have just been reported and on which is founded the theory of the indirect action of radiation on cancer, there are only a few, as we have seen, the results of which have not been contradicted. But even if they had all been confirmed, there would still be a few criticisms to offer against them.

(*a*) They all relate to *grafts.* The extension to spontaneous cancer of the conclusions of experiments conducted with tumors transplanted to mice or rats should be made only with extreme caution, even though these grafts are autogenous grafts of spontaneous cancer. *The success or failure of transplantation does not signify receptivity or immunity with regard to cancer, but only with regard to grafts in general;* so also, the results obtained on transplanted tumors, either by a physical or medicinal agent, or by a dietary regimen, do not signify cure, or failure to cure, cancer, but a positive or negative effect on the tolerance of a graft (which is usually taken from a neoplastic

tissue, but which might just as well be taken from a normal tissue). In reality, the technic of grafted cancer has permitted us to study the physiology of the graft rather than that of the cancer.

(*b*) Many of these experiments which have been regarded as demonstrating the indirect action of radiation, may, on the contrary (because they utilize grafts as material), be interpreted as supporting the direct action. For example, the fact that a normal fragment of tumor implanted in an irradiated region does not develop, may be explained just as well by a direct action of radiation on the general tissues of that region, rendering them unsuitable to furnish in the graft the formation of new vessels and stroma, a condition which is essential for the survival of the differentiated cells of the transplant.

(*c*) Another argument has had much weight in favor of the indirect action. It is necessary to administer very strong doses —doses much stronger than those used in the treatment of cancer, to a fragment of tumor, irradiated *in vitro* in order that a transplantation may be negative. A certain number of the experiments which I have reported have been, indeed, carried out by irradiating *in vitro* fragments of tumor which were grafted after irradiation—Chambers and Russ (7), Murphy and Morton (36), Murphy, Maisin, and Sturm (34), Kok and Vorlaender (25), and Nather and Schinz (38); or, again, by irradiating, before transplantation, the tumor *in situ* in the body of an animal previously killed—Keysser (24).

The necessity of strong doses (which, however, vary with every tumor used) proves first of all the relatively slight sensitivity of many of the tumors of mice and rats. The malignant tumors of these animals appear to be generally more radioresistant than human cancers, according to Wood and Prime (56). It may also prove that the sensitivity of cancer cells irradiated *in vitro* is less than when they are irradiated *in vivo*. Loeb (29) had already formulated this hypothesis with the following arguments: Freezing and deprivation of oxygen diminishing the activity of irradiated tissues and reducing the efficacy of rays on the cells; besides, there is deprivation of a part of the scattered radiation.

Wood (54), on the contrary, thinks that the lethal dose for cancer cells is slightly lower if the irradiation takes place *in vitro*.

As for normal tissues, the experiments of Jolly (17, 18, 19), of Ferroux, Jolly, and Lacassagne (12), and Ferroux and Regaud (13) have established that the interruption of circulation reduces appreciably the radiosensitiveness of the cells of an organ. It seems as if the same is true of cancer tissue, as is shown by the following unpublished experiment carried out by Samssonow and myself.

From a rat bearing two tumors, one on the right, the other on the left, obtained by grafting a fibrosarcoma, we extirpated one of them (*B*) and, through a buttonhole incision in the skin of the flank, we introduced it into the vicinity of the tumor (*A*) of the other side, taking great care not to injure the blood supply of the latter. The two tumors were irradiated simultaneously.[2] Immediately afterwards we inoculated into six other rats a double graft on one side with sarcoma *A*, the circulation of which was maintained during the radiation; on the other side with sarcoma *B*, the circulation of which was interrupted during the irradiation. One of these animals died during the next few days. In the five others the grafts with sarcoma *A* were all negative; those made with sarcoma *B* all produced tumors which developed progressively, although their growth was retarded.

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[2]Conditions of irradiation: Skin target distance 30 cm.; filter 5 mm. aluminium; equivalent spark between points 40 cm.; current intensity 5 ma.; time 1 hour; dose 20 *H*-units.

From the results of this experiment the argument that "the dose necessary to make a tumor disappear *in vivo* is smaller than that required to sterilize a graft outside of the organism" can not be adduced against the direct action of radiation.

(*d*) Finally it may be useful to recall, without insisting on it, that many of the conclusions drawn from the radiation experiments on small animals (where irradiation with purely local effect is very difficult to achieve) are in direct contradiction to the teachings of the clinical results in human beings. Unfortunately, we do not see lymphatic involvement or untreated metastasis disappear after cure of the primary lesion; on the contrary, we sometimes have the impression that their growth is accelerated. And do not local recurrences usually occur at points where a poor distribution of radiation has not allowed the administration of a sufficient dose?

SUPPOSED MECHANISM OF THE INDIRECT ACTION OF RADIATIONS

One may group into two principal theories the conjectures advanced by the advocates of the indirect action of radiation with respect to the mechanism of such action.

I shall designate the first by the name of *Lymphocytic theory.* Immunity in general should be a function of the number of lymphocytes and these elements should play the principal rôle in the defense of the organism against cancer; the refractory state (natural or acquired) should be accompanied by lymphocytosis, and lymphopenia should allow a return of receptivity; the tolerance or the absorption of a graft should be explained by the absence or presence of lymphocytes in or around it. By permitting the ready modification of the lymphocytic formula of the blood, radiations constitute an experimental agent of the first order, thanks to which, we can, at will, render an organism refractory or receptive to cancer. Their action in the treatment of this affection is then nothing but the measure of their action on the lymphoid elements.

Murphy and his collaborators, Russ and his co-workers have been the principal champions of this lymphocytic theory. To its support these two schools have brought forth numerous exact experiments, carried out methodically and with perseverance, which, for this very reason, lend themselves to discussion and criticism.

I have indicated, in connection with each experiment in particular, the refutations of it which have been made. Moreover, Wood (53), who obtained taking grafts in leukemic animals under the same conditions as the controls; and Keller (23), by showing that transplanted tumors develop well in the peritoneal cavity of mice, which is particularly rich in lymphocytes, have brought forth against this theory original and serious arguments.

The second theory may be called the *Stimulation theory.* It came to light at the time when many radiotherapeutic schools accepted as fact the existence of definite doses for sterilization, notably of carcinoma and sarcoma. Under these conditions there was reason to be worried by the result of the experiments of Keysser (24), of Kok and Vorlaender (25), and Nather and Schinz (38). If, for example, a mouse carcinoma was irradiated before transplantation and produced a malignant tumor in spite of the administration of doses four or five times greater than the Karzinomdosis, it was because the cancer cells were not killed by the rays. Their disappearance, in a tumor irradiated *in vivo* with much lower doses, could be very readily explained by a reaction of the host stimulated by the rays (providing the dose was not too strong, in which case the defense of the organism might be destroyed). I have stated in the preceding

paragraph the answer which can be given to this argument.

But how could the rays produce this favorable reaction in the organism? For the majority of authors there is, first of all, a local action on the connective tissue in which the rays excite the function of the fixed and mobile cells. This mechanism is therefore essentially that which was already admitted by Bashford, Murray, and Cramer (4). But to this reaction of local defense there is added a general reaction on the explanation of which the authors vary. According to Caspari (6) the destruction of a certain number of cells as a result of the irradiation of the tissues liberates certain non-specific products, "necrohormones," which, besides a local action, provoke, after passage into the blood, toxic effects and call into play the general form of immunity. There is here, as one can see, a reminder of the old theory of Schwarz (45), according to which the rays decompose the cholesterin of the tissues and liberate a toxic product; and especially of that of the cytotoxins of Baermann and Linser[3] (3).

According to certain authors, such as Fraenkel (14) and Slosse and Reding (48), cancer is a general disease secondary to dysfunction of certain glands of internal secretion and the rays act on these glands to modify their secretions.

Opitz (39) supposed humoral modifications from colloidochemical disturbances were provoked in the tissues by radiation, the result of this being an excitation of the reticulo-endothelial system. This, held under control by the vegetative nervous system, the "vital nerves," the glands of internal secretion, and the gray nuclei of the third ventricle, calls forth the reactions in defense against the cancer cells.

From these examples, we see that all the physiologic mechanisms still under investigation (cellular ferments, disturbances in cellular exchanges, glandular hormones, the vegetative nervous system, reticulo-endothelial system, etc.), particularly the most obscure, have been invoked to support the theory of the indirect action of radiation on cancer. Manifestly no demonstration of such hypotheses has been made.

However, it is important to say a few words about an objection which touches all the theories, according to which the cure of cancer by radiation is due to the aid which it brings to the organism in its defense against cancer. *Does there exist a defense of the body against cancer?*

The debate on the reality of such resistance which has been going on for such a long time among cancerologists is not settled even now.[4]

The principal arguments of the partisans of this hypothesis are well known: There exist cases of spontaneous cure of malignant tumors; leukocytic reactions which coexist with appearances of disintegration or tolerance of cancer cells are observed histologically around neoplastic formations of certain cancers, and we also find fibrous hyperplasia surrounding and appearing to choke off the neoplasm and thus retard its growth.

In reality, all the rare cases of spontaneous cure of malignant tumors contain loopholes and inaccuracies which make their authenticity doubtful. Strauss (50) has recently made a critical study of such cases. On the other hand, the failure of numberless attempts at immunization in man, and the impossibility of curing a malignant neoplasm by a serologic substance, either organic or medicinal, are hardly in favor of a

[3]Regaud: Bull. Acad. Med., 1924, XCI, 604, in order to explain the progressive radio-immunization of certain cancers, advanced the hypothesis that irradiated collagenous substances are probably the origin of a cellular toxin, the production of which is exhausted by repeated irradiation.

[4]See on this subject the two reports presented to the Strasbourg Congress on Cancer (July, 1923) concerning "the local and general reactions of the body to cancer," the one by Rubens-Duval, the other by Wooglom, the conclusions of which are exactly opposite.

resistance of the organism to the invasion of the tumor to which it supplies nourishment.

It has been established for a long time that histologic examination often shows leukocytic infiltration around neoplasms, notably in the supporting tissue of many epitheliomas. Such infiltration varies in the cells of which it is composed (sometimes polymorphonuclear, sometimes purely lymphocytic, or plasmacytic or eosinophilic, or even sometimes mastocytic) and is of uncertain interpretation. In certain cases, such leukocytic infiltration may obviously depend on the microbic infection associated with many ulcerated tumors. In other cases, we might ask if they do not represent evidence of a local inflammatory condition, antedating the cancer, and having led to its development; in fact, it should be noted that the same changes in the supporting tissue cannot be found in invaded lymph nodes and in visceral metastases. There even exist tumors, such as lympho-epitheliomas, for example,[5] in which the lymphocytes are living literally in symbiosis with the neoplastic cells, and the malignancy of which, nevertheless, is very great. Finally, many varieties of tumors are made up of cells of very great fragility, and the microscope usually shows among them a large number of elements undergoing spontaneous necrobiosis (moreover, the incessant renewal of cells is one of the characteristics of malignant tumors). Under such conditions local leukocytic infiltration is a physiologic phenomenon, and we take cause for effect when we interpret the cellular degeneration in cancerous formations as secondary to the presence of leukocytes in their supporting tissue.

We see that the theory of the defense of the organism against cancer is even to-day nothing but "an article of faith." Any interpretation of the action of radiation on cancer based on the stimulation of the reactive processes of the organism rests, therefore, on a very slender basis.

THERAPEUTIC CONSIDERATIONS AND CONCLUSIONS

The theory of the indirect action of irradiation was naturally to lead to new adaptations in the radiotherapy of tumors.

I shall not insist on the attempts at immunization by injection of cancer tissue treated by irradiation; these are as ineffective as the many previous attempts to inject tumor extracts. Following the experiments of Kok and Vorlaender (25), which apparently establish the fact that a weak dose of radiation administered to the body as a whole is much more effective than a strong dose received by the tumor, general irradiations have been tried. So-called stimulating radiotherapy of the spleen or different glands has been combined with local irradiation. It does not seem as if these trials have furnished convincing results in human therapy. It is true that Opitz (39) has called attention to certain cases in which the tumor has disappeared after very small doses and other cases in which cancer cells have persisted in the midst of a connective tissue destroyed by excessive irradiation. The difference in radiosensitivity of the many varieties of malignant tumors suffices to explain these apparent contradictions.

On the contrary, numerous facts unfavorable to the indirect action have been reported. I shall cite only the case of a mammary epithelioma *en cuirasse*, published by Juengling (22), in which histological examination showed the persistence of cancer cells in only a narrow zone which the interposed lead had protected against the direct action of the rays; and also the fruitless attempts of Baensch (2), who did not succeed in influencing cancers by all radiotherapeutic measures other than direct irradiation.

Finally, from a comparison of the statistics published by the principal establishments

[5] The lympho-epitheliomas of the pharynx, according to Jovin in Ann. des maladies de l'oreille, du larynx, du nez et du pharynx, 1926, XLV, 729.

specializing in the radiotherapy of cancer, it appears that the results obtained in those where local radiotherapy is practised exclusively are not inferior to the results obtained by establishments where direct irradiation is systematically combined with any irradiation, the object of which is to produce an indirect effect.

The development of the preceding ideas authorizes me to continue to state, even today, that, *if radiation causes tumors to regress, it is because it injures their cells directly and electively,* and that, if we succeed in curing certain tumors, it is because their cells are more radiosensitive than the cells of the normal surrounding tissues.

Does this mean that we should limit our efforts to the administration of what we believe to be the lethal dose for cancer cells, without taking the trouble to preserve the integrity of the general tissues? Much to the contrary, such a course of reasoning can not be that followed by those who believe in the great differences in the radiosensitiveness of tumors.

By taking care of the normal tissues as much as possible, it becomes feasible to cure a greater number of slightly radiosensitive tumors. Do we not, thanks to the artifice of multiple ports of entry, succeed in killing cancer cells much less radiosensitive than the cells of the epidermis? By safeguarding the general tissues, we seek to produce a more rapid cicatrization, a relative integrity, which permits us to avoid immediate or late accidents.

Thus, in spite of the conviction that the action of radiation on cancer cells is a direct one, I will say even because of this conviction, one of the directing principles of the work at the Radium Institute of Paris has consisted in perfecting technical procedures with the idea of taking care of the normal tissues: heavy filtration, single treatment, prolongation of the time of irradiation, and reduction of the intensity, permanent interruption of irradiation at the moment of onset of the period of repair, disinfection of ulcerated tumors, etc. These different technical procedures all lead to the realization of what continues to be the essential factor for success in the radiotherapy of tumors: the administration to all the tumor cells of the strongest dose compatible with the integrity of the normal tissues.

CONCLUSIONS

1. Three principal theories have been maintained to explain the destruction of cells under the influence of radiation: (*a*) a direct action, (*b*) a local indirect action, (*c*) an indirect general action.

2. This problem can be regarded as solved in so far as it concerns the normal elements. Radiation exercises its elective effects directly on the cells, and the indirect action is no longer considered, even by those authors who admit it only as an accessory phenomenon.

3. So far as pathologic tissues are concerned and especially cancer cells, the problem presents itself under more obscure conditions.

The many experiments undertaken with transplantable rat or mouse tumors with the idea of showing an indirect action have, for the most part, been contested; even if they were all recognized as sound, serious objections could still be opposed.

4. Clinical teaching and the results of therapy lead us to believe that, in cancer, as in normal tissues, radiation acts by damaging the cells directly and electively.

5. If the goal of the radiotherapy of malignant tumors should above all be the destruction of the neoplastic cells, the importance of preserving the general tissues should not be forgotten. By attaining these two objectives we follow a line of attack formulated long since, which seems to be the most important condition for success: to administer to all the cancer cells the

strongest dose compatible with the integrity of the healthy tissues.

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REVIEW OF VARIOUS METHODS OF TREATMENT OF CARCINOMA OF THE CERVIX[1]

ATTENDANT PRIMARY MORTALITY AND FIVE-YEAR CURES

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In order to attain the highest degree of efficiency in the treatment of any particular disease, it would seem to be necessary to check up periodically not only on the therapeutic measures commonly employed, but also on the results brought about by their use. By this means only, can we intelligently discard the doubtful or useless procedures, concentrate upon or modify the measures productive of the greatest salvage, or even, when necessary, adopt more promising, entirely new methods. In no instance is this more true than in the case of the elusive cancer of the cervix uteri.

Carcinoma of the cervix, it has been claimed, is "the most frequent type of neoplasm in the female genital tract," so that unfortunately there has been no dearth of material for study. In the face of this, contemplation of the history of the treatment of cervical carcinoma for the last twenty years leaves one with the discomforting realization that the measures employed against this common scourge apparently always have been, and certainly still are, surprisingly inadequate.

One of the earliest agents of destruction, in common use twenty years ago, was zinc chloride. The treatment consisted in thorough curettage of the growth, sometimes followed by cauterization with heat. This in turn was followed by the local application of a gauze bag containing a paste made of 50 per cent zinc chloride in starch. This mixture was firmly pressed and moulded into the cervical growth. In order to protect the vaginal vault, the bladder, and the rectum, the paste was surrounded by smaller bags filled with bicarbonate of soda. These bags were held in place by a gauze tampon and by a firm T-bandage. The vagina was emptied in twenty-four hours and a soda douche was administered. This treatment was followed by a great slough of carcinomatous tissue and sometimes by a rectovaginal or vesicovaginal fistula. On the other hand, as a palliative measure, in some instances the results were surprisingly gratifying. The primary mortality was practically *nil* and a five-year cure was heard of occasionally. It should be noted that microscopic sections were by no means a universal procedure and probably all of the few, well authenticated five-year cures were of the epidermoid type, belonging to Class I or II of Broders' classification. Furthermore, allowance should be made for possible diagnostic error.

At this time also, the ordinary panhysterectomy, with removal of both tubes and ovaries, was in vogue for less advanced cases. The primary mortality ranged from about 5 to 10 per cent, depending to a considerable extent on the degree of advancement in the particular case. Sometimes hysterectomy was preceded by cauterization with the actual cautery, as originally suggested by Byrne, of Brooklyn, in 1892, and many times this type of cauterization was used exclusively. From cauterization alone there was no primary mortality, but, on the other hand, there were few if any survivals for the five-year period.

Among the other comparatively less formidable surgical procedures, there should be noted the technic of Percy, described in 1912; also the bilateral internal iliac and ovarian ligations plus Percy cauterization, advocated by S. M. D. Clark, in 1915, and,

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 28–Dec. 2, 1927.

besides, the intravenous administration of colloids.

Percy's technic, you will recall, was based on the idea that a low degree of heat, sufficient only to desiccate without charring, would penetrate more deeply and therefore produce more extensive destruction of carcinomatous tissue. He also demonstrated that even this low heat (110–115 degrees) was capable of destroying carcinomatous cells, without also injuring normal tissue cells adjoining, especially if the latter were adequately protected. The practical application consisted of retraction of the vagina with a water-cooled speculum through which the so-called "cold iron" was applied. During this procedure the degree of heat was controlled from the abdominal side by means of the hand or a thermometer. The primary mortality was about the same as for simple laparotomy. As a palliative measure, the technic had undoubted merit. In so far as five-year cures are concerned, accurate statistics for a large group of cases are difficult to obtain for the reason that so many victims were already hopelessly advanced when operated upon.

In large cervical growths, as a preliminary step to the application of radium, this type of cauterization has a definite field of usefulness, even at the present time. It may furnish the means of disposing of an exuberant growth which prevents the application of radium in sufficiently close proximity to the base of the cervical tumor. In such a case it may not be essential to carry on the desiccation to the point where it becomes necessary to control the heat from the abdominal side.

Clark, of New Orleans, used Percy's procedure with a fair degree of success in converting a certain proportion of borderline cases to the stage where they were suitable for the Wertheim hysterectomy. His modification consisted in doing a preliminary ligation of both ovarians and both iliacs. This was followed by a Percy cauterization and later by a Wertheim hysterectomy in suitable cases. Statistics as to five-year cures are not available.

In connection with the intravenous treatment of cancer, it is interesting to note that as early as 1769 lead was advocated as a local treatment for cancer. The publications of Wassermann in 1911 stimulated experimentation with colloids in both animals and humans. In 1912 while Leo Loeb of the Skin and Cancer Hospital of St. Louis was experimenting on mice with colloidal copper, Dr. Maurice Couret and myself treated a number of cases of inoperable cervical carcinoma. The results did not justify publication for fear that more harm than good might ensue from the broadcasting of these experiments. As in many new methods, the initial results seemed to be brilliant but later the treatment apparently gave impetus to the growth and was fraught with many other dangers. Further observation only strengthened our conviction in this matter.

In 1920, Prof. Blair Bell began his treatment with colloidal lead compounds. This consisted essentially in the intravenous administration of approximately six hundred milligrams of lead over a period of about six months. From this work it appears that no type of cancer is especially susceptible, though slow-growing tumors, like basal cell epitheliomata, are apparently not affected, probably on account of their low vascularity. On the other hand, rapidly growing, vascular tumors are more susceptible to lead, just as they are more susceptible to radiation. Of all types of carcinoma, 80 per cent are uninfluenced and the remaining 20 per cent are more or less benefited. Experimenters believe that of this number a small percentage "will be apparently cured" after three or five years. This leaves us for consideration the radical surgical procedure

by the vaginal route and by the abdominal route, and finally the treatment by radiation.

The two radical surgical operations have attracted so much attention, for various reasons, that minute details of technic need not be given here. The fundamental idea underlying both the vaginal operation and the abdominal, is that at some time or other cervical cancer is purely a local disease, and, therefore, if operated upon at this time, it is amenable to cure by a wide extirpation of all tissues surrounding it. So that in both these operations, the degree of advancement of the cancer plays an important part in determining the results obtained. The most popular radical operations are the vaginal hysterectomy of Schauta and the abdominal hysterectomy of Wertheim. There are certain points of interest as regards these two operations.

Wertheim began his work in 1897 and his operation was developed and popularized by the suggestions of Clark, Riess, Worder, Doederlein, Bumm, Proust and others. Wertheim has reported in a series of eight hundred cases 42 per cent of five-year cures. Berkeley and Bonney have reported about 25 per cent cures and Kroenig and Doederlein about 20 per cent. The only figures of really practical value, however, are those offered by the results obtained in large numbers of cases, done by many operators. Therefore the average primary mortality and five-year cures have been computed from the sources quoted by John G. Clark.

In determining the primary mortality and five-year cures from operation, so many factors come into play that, even in dealing with large numbers of cases, there are considerable discrepancies in the figures. For instance, Duncan found that in 1,720 cases operated upon by the abdominal route there was a primary mortality of 18.23 per cent and a percentage of five-year cures of 19.32 per cent. For the vaginal route, the primary mortality in 654 cases was 9.35 per cent, and the five-year cures 17.74 per cent. The statistics of John G. Clark, based on the work of ten of the large clinics of the world, give a more accurate idea of the five-year cures in radical abdominal hysterectomy. He found in striking an average from the figures of Martzloff, Mayer, Cobb, Graves, Bonney, Peterson, Schweitzer, Davis, Giesecke, and Bumm, that in 1,539 abdominal operations there was a primary mortality of about 15 per cent and a curability of 39.5 per cent.

Considering the tremendous technical effort put forth in radical operation and the high toll exacted in lives which operation entail, 39.5 per cent of five-year cures seems but a small remuneration to compensate for strenuous efforts. And yet for the very rare, early cases of cervical cancer, radical hysterectomy would seem to be the logical procedure, especially in adenocarcinoma, when the tumor has not extended beyond the cervix.

And now, as a competitor of surgery, what has radiation to offer?

Radiation by deep therapy exclusively does not seem to be particularly well adapted to the treatment of cervical carcinoma, and so far, in this country at least, has not come into popular favor for this purpose. However, as an adjunct, deep therapy does have a definite field of usefulness, particularly in the control of metastases, extending over large areas. No statistics as to five-year cures by deep therapy alone have been available to us.

Radiation with radium, however, is especially suitable for the treatment of cervical carcinoma. On account of the high primary mortality and comparatively low five-year salvage, the last few years have seen many converts from the ranks of the surgeons, who have turned almost entirely to radium, except for the comparatively rare, early cases.

As to curability from radium, Clark of

Philadelphia, one of the converts, has shown from analysis of the figures of Burnam, Flatau, Bailey and Healy, Schmitz and Bumm, that radium gives a curability of 43 per cent as against 39.5 per cent by radical operation. The salvage, therefore, is practically equal, but the great difference lies in the primary mortality. It is true that the statistics of Heyman, Saltau, Norris and others are not so favorable to radium, but the figures compiled by Clark are probably more nearly correct, as they are based on the results of individuals having at their command large quantities of radium.

In conclusion, one finds it difficult to leave the depressing subject of cervical carcinoma without reiterating the hackneyed plea in behalf of prophylaxis. Since we find it so difficult to dispose of carcinoma once it has made its appearance, it becomes our duty to cut down the incidence of cervical malignancy by redoubling our efforts against its precursors. The principle of disposing of all points of chronic irritation has been amply proven, and in the case of the uterine cervix, the correction of lacerations, endocervicitis, metaplasias or erosions is still a crying necessity.

A word of thanks for valuable assistance in preparation of this paper is due Miss Marie Louise Marshall, Librarian of the Orleans Parish Medical Society, and to Dr. Adolph Jacobs of New Orleans.

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DISCUSSION

Dr. Albert Soiland (Los Angeles): There is a statement emanating from many sources to be read in the scientific and in the public press, that cancer is approaching a solution; that we are gradually approaching a point where the veil will be torn aside and we will learn the mysteries of cancer. I am sure that we are all anxious for that moment to arrive, and I believe that this symposium has brought that statement a little nearer the truth. The statistics which Dr. Gelpi quoted are as reliable as can be compiled at the present time. The treatment of carcinoma of the cervix is pretty well established to-day —that is, radiation comes first and surgery comes second. In view of present developments, I do not believe the type of surgery mentioned as bearing the name of a certain individual (no personal reference is intended) is scientific as an entity. It is rarely used in the type of case for which it was designed, but is too often used for major surgery, where its use is attended by great danger to the patient.

With reference to colloidal lead—one year ago my associates and I presented a report on our year's experience with colloidal lead. At that time we were imbued with the hope —the expectation which Bell conveyed in his paper—that massive doses of colloidal lead might prove curative. We were disappointed in our results. We tried it out in a sufficiently large number of cases, but were unable to duplicate or even approach Professor Bell's results. However, we did not entirely lose faith. We have persisted in the use of colloidal lead, and are employing it to-day in conjunction with our work in radiation. We give small doses of colloidal lead phosphate, as perfected by Bischoff, of Santa Barbara. This is less toxic than the original metallic colloid, and is more compatible with our work of irradiation. I trust to be able to give you some tangible reports on the results of this work in the not-too-distant future, and I believe they are going to be better than the last report we made.

Dr. H. Holthusen (Hamburg, Germany): Of the numerous questions discussed by the different speakers, I wish to come back to the question raised by Dr. Lacassagne about the direct or indirect effect of radiation. I quite agree with his very critical standpoint relative to the indirect effect of rays, still, I want to ask him whether he does not believe that there is a possibility for indirect effect, considering, for instance, the experiments which show that by an injection of colloidal substances one can bring a tumor to an involution, or whether he thinks that these experiments do not hold because they are effective only on animals which have received tumor grafts. At any rate our clinical experiences prove—and there I quite agree with Dr. Lacassagne—that the direct effect of the X-rays prevails, and I think the most striking experiment is always that which can be carried out in irradiating a skin metastasis. There the effect is always limited, even in the limits of one millimeter to the irradiated area. The prevailing direct effect can be shown also by the fact that the difference in the susceptibility for rays varies with the kind of cells; taking, for instance, the seminoma, on the one hand, and the squamous cell carcinoma on the other. I believe these questions are very important from the standpoint of practical therapy. Our possibilities do not lie in the direction of varying the quality of rays: Dr. Wood has shown that, independent of the wave length, the same amount of ionization has the same destructive effect on the cancer cell. I believe that future success lies in the proper working out of the time distribution of the radiation, and this is the phase of the problem which we have to take up and to improve.

DR. GELPI (closing): I wish to say only a few words about the cautery. Dr. Soiland, I do not want you to misunderstand me; this was a sort of historical paper and the cautery was mentioned as we went along, describing the various therapeutic procedures which have been used. What I did say in connection with it and what I meant was that in the large cervical growths, preliminary desiccation of the exuberant mass with the "cold cautery" has definite value. If you implant radium in such a soft, friable, sloughing mass, always extending for a considerable distance from its origin in the cervix, you are not going to accomplish very much. On the other hand, if you take an electric cautery and apply it with a low degree of heat, all this excessive mass can be disposed of at one sitting, and then you are at the bottom of your carcinoma, where you can apply your radium efficiently. It was not my idea to recommend it exclusively, in place of either surgery or radiation.

DR. MACCARTY (closing): I just want to emphasize one thing which Dr. Wood touched upon. He said it was dangerous for pathologists to diagnose cancer on a single cell. I want to emphasize exactly what he said: *It is dangerous.* One of my associates, whose name has been mentioned here two or three times to-day, was trained over a period of four years before I would allow him to make a diagnosis; that was Dr. Broders. Another thing I want to mention that has been spoken of. I do not like to hear our clinicians apologize in the presence of so-called scientific men. What is the real test of whether a thing is malignant or not, and who knows about it? If there is any one here in this audience who knows that any of my diagnoses are wrong, I hope he will tell me about it. The term "malignant" to me is a clinical term. I know one or two pathologists who will not agree with that, but to me the term "malignant" is always a clinical term, and if I say the patient has cancer, I want you to follow the case and tell me later how long the patient lives and, if dead, what he died of. Now the figures I gave you to-day, covering a period of eleven years, were not worked up by me; they were worked up by professional statisticians from my material, and, by the way, this same material is being worked up by another statistician (Alvarez) according to his way of doing it. I only make observations, and I put them down. If you ask me my opinion about a thing, I tell you whether I think it is malignant or not and just how malignant it is, if possible.

To-day I have merely presented results of observations over a long period. I was making a biological study of human beings and Dr. Wood was doing the same thing on lower animals. It is only by such observations and the comparison of results and material that we are going to progress. I am thoroughly in accord with Dr. Wood's attitude and I suspect that he might be in accord with mine—he is probably glad that I have so many thousands of human beings to study. I certainly am happy that he has so many thousands of lower animals to study. In the few years I have been coming to your Society, and this is my third trip, I have seen a change of attitude toward many scientific and clinical problems; the change is a constructive one; your Society is getting better every year; it is getting more scientific and also more scientifically practical. The greatest test of science lies in its practical application.

RADIOGRAPHY OF NORMAL LARYNX[1]

By P. M. HICKEY, A.B., M.D., ANN ARBOR, MICHIGAN

RADIOGRAPHY of the larynx has been studied mostly by Continental workers. The "Atlas," of Thost, probably represents the most important contribution so far presented. We would mention also Iglauer and Lange in this country. The present study was undertaken as a contribution to a subject somewhat neglected. The refinements of modern technic, permitting of a rapid exposure, have simplified the subject in a very decided manner.

The larynx is capable of four types of movement: first, movements from the action of the muscles of the neck producing displacement of all the structures of the neck; second, displacement by the intrinsic and extrinsic muscles of the larynx; third, movements incident to respiration, and fourth, blurring due to the cardiac impacts transmitted by the carotids.

For the successful elimination of these various types of movement, it is not sufficient to ask the patient to suspend respiration and keep as still as possible. It is necessary to employ flash exposures. Most of the studies which the writer has made have been accomplished with an exposure of a twentieth of a second, the exposure being made with the help of a relay circuit breaker actuated by an overload of the primary. The time of these exposures was verified by means of the timing top.

Naturally, the maximum amount of information is gathered from a lateral exposure, the antero-posterior being of little value on account of the overlying shadows in the cervical vertebræ. The lateral exposure may be made on a 5×7 film in a cassette with a narrow edge. A cassette of larger size with a wide edge is inconvenient and the wide edge will often cut off part of the tissues under examination. With a small 5×7 cassette the film can be accurately placed so as to show the shadows of the laryngopharynx, the larynx, the trachea for some two or three inches, the upper portion of the esophagus, and the cervical vertebræ.

Usually, the amount of the trachea which can be shown will depend upon the body habitus, more difficulty being experienced with patients with a short neck. The skin target distance should be at least 30 inches, preferably 36 inches. In patients with a short neck and in cases where one desires to include as much of the trachea as possible, the larger cassette, an 8×10 or a 10×12, may be supported beyond the shoulder and the tube removed to a distance sufficient to minimize the enlargement. Incidentally this technic, introduced by Caldwell many years ago, is very successful in the demonstration of the cervical vertebræ. This second procedure is better carried out with the patient sitting up and grasping the seat of the chair so as to pull the shoulders down on each side as far as possible. The head should be supported in an erect position by a non-radiopaque pillow. It will be necessary to increase the length of the exposure to compensate for the greater distance.

Over-exposures should be carefully guarded against and the kilovoltage should be kept as low as possible in order to secure the maximum contrast in the soft tissues. An exposure which may portray well the cervical vertebræ may be entirely unsuited for displaying the laryngeal structures.

The radiologic examination of the larynx is oftentimes of importance in studying the changes produced by benign neoplasms, carcinoma, and tuberculosis. Before taking up

[1]Read before the Radiological Society of North America, at the Thirteenth Annual Meeting, at New Orleans, Nov. 28-Dec. 2, 1927.

the study of pathology of the larynx it is necessary to become thoroughly familiar with the appearance of the normal.

In the lateral projections of the larynx we may consider first of all the supralaryngeal structures; of these, the air column in the laryngopharynx is usually conspicuous, its anterior boundary being the base of the tongue and its posterior boundary the posterior pharyngeal wall. Prominent among the structures in this area is the hyoid bone, which shows in rudimentary fashion during the first year of life, the body of the hyoid being the only part visualized. Later, the greater horns of the hyoid appear, producing a horseshoe shadow. The lesser horns of the hyoid are usually inconspicuous and recognized with difficulty. In the lower part of the laryngopharynx, the epiglottis is conspicuous, to be recognized by its broad base and tip, which curls anteriorly. While cartilaginous, it is differentiated by the fact that its shadow is projected against air background. Later in life we find definite lime deposits in the lower third. These are usually arranged in small rings, giving oftentimes the appearance of small perforations.

The thyroid cartilage up to the age of puberty is differentiated with difficulty. The development of the thyroid cartilage in the two sexes proceeds in about the same fashion until puberty, after which the thyroid cartilage in the male develops much more prominently. The deposit of lime within the thyroid cartilage is somewhat irregular, the densest shadow being found at the junction of the anterior and lower border. In the female the deposit of lime in the thyroid cartilage is inconspicuous.

The cricoid cartilage forms the shadows well below the glottis and presents characteristic appearances in the male and female laryngeal shadow. In the female after the age of twenty, the deposits of lime occur principally along the posterior border, the deposits being laid down in somewhat regular fashion with a definite center and a peripheral shadow which is less distinct.

The arytenoid cartilages can often be distinctly recognized as small triangular shadows situated along the posterior border of the larynx, but later are overshadowed by the deposits in the cricoid. The glottis can usually be made out distinctly, as the glottic opening is distinct during quiet respiration. The glottic shadows should always be carefully studied, as pathologic infiltrations will alter its usual appearance.

In general, we may state that the male larynx is distinguishable from the female larynx by the greater lime deposit of the thyroid cartilage in the male; in the female the thyroid shows only a very slight lime deposit, while the cricoid is usually conspicuously outlined.

During phonation the position of the epiglottis will vary according to the vowel which is uttered and the glottic opening will assume an appearance corresponding to the tension and position of the vocal cords.

In studying the phenomena of swallowing, we note, first of all, the position of the hyoid bone, which is sharply drawn up so that it is much nearer the shadow of the lower edge of the mandible. The epiglottis becomes indistinct on account of the fact that it is pushed downward and backward by the base of the tongue against the posterior pharyngeal wall. The entire laryngeal shadow, following the pulling up of the hyoid, is much higher. The valleculæ of the larynx are seen only in studies made with the barium meal. During the swallowing of a fluid emulsion of barium, the valleculæ will be seen to form crescent-shaped shadows on either side of the larynx as viewed in the postero-anterior projection. As the emulsion passes down, it separates and fills the pyriform sinuses on each side.

With every gastro-intestinal meal exami-

nation the entrance of the barium emulsion into the pharynx and then on into the esophagus should be noted, so that one may become familiar with the physiologic aspect of the act of swallowing. Only by becoming fairly familiar with its appearance, will mistakes be avoided in the recognition of upper esophageal pathology.

DISCUSSION

DR. SAMUEL BROWN (Cincinnati): It was a delight to listen to Dr. Hickey. I have been waiting for this paper since May. In Washington I met Dr. Hickey and spoke to him about this work and told him I was also interested in it. I went home and began to use it frequently and I am enthusiastic about the method, because it has proved of very practical use to me. The difference in my method and Dr. Hickey's is a difference in distance. Dr. Hickey, I notice, takes the film close to the neck. No doubt a film like that will give one much better detail than a long-distance film. My work is always taken at a distance. That magnifies the shadow, but perhaps brings out certain details more distinctly. I have especially found a great deal of information as regards the trachea and its relation to the thyroid cartilage. Some of you perhaps have noticed the exhibition outside of films of the neck, showing the larynx and the trachea and the relation to the thyroid. The larynx is more or less calcified according to the age, and it was surprising when Dr. Hickey approached me and told me the sex and approximate age of each individual; I did not know how he could tell, as he had not seen the patients, but he called my attention to the difference in the calcification of the larynx. I am glad I have learned that. As regards the trachea, you will notice that I was able to visualize any deviation. Under normal conditions one finds the two walls parallel to the spine. When the thyroid gland is enlarged it will produce deviation of the trachea. Several patients were operated on and every diagnosis was proven to be correct.

BRONCHOGRAPHY ACCORDING TO THE PASSIVE TECHNIC: THE METHOD OF CHOICE FOR THE ROENTGENOLOGIST[1]

By ALTON OCHSNER, A.B., M.D., F.A.C.S., New Orleans

UP to the time of the discovery of the X-ray by Roentgen, in 1895, diagnoses were made only by history and physical findings. While it is undoubtedly true that clinicians at that time trained their own special senses better than the average present-day clinician does, yet, even with this high training of special senses, many mistaken diagnoses were made. This was true not only of the osseous system, but also of the gastro-intestinal, genito-urinary, pulmonary, and cardio-vascular systems.

Following the clinical application of the roentgen ray, the percentage of correct diagnoses which were made immediately rose. Those structures which were dense enough to cast a shadow on the radiographic plate, such as the osseous system, were most readily studied. In order to visualize the hollow viscera, it became necessary to introduce opaque substances which would show on the X-ray plate. Lesions of the gastro-intestinal and genito-urinary systems, which previously had not been suspected—especially in the early stages—now could be diagnosed, because an alteration in the normal outline of the hollow viscera was easily made out. It was soon found that in those viscera where rapid change in the contents was apt to take place the fluoroscopic observation of the contrast substance within the viscus was more desirable than merely the interpretation of the X-ray plate. This was especially true in studying the gastro-intestinal tract, particularly the stomach and duodenum. Radiologists came to realize that no gastro-intestinal examination would be complete without a fluoroscopic observation of the stomach and duodenum with the contained barium meal. Because of the rapid changes which may occur during the passage of food through the stomach and duodenum, considerable valuable information is lost if the stomach and duodenum are not examined under the fluoroscopic screen.

In order to better visualize the outline of the tracheo-bronchial tree, Jackson, in 1905, insufflated bismuth oxide into the tracheo-bronchial tree through the bronchoscope. Because of the irritation which it produced, bismuth oxide was soon replaced by bismuth subcarbonate. In 1917 Yankauer applied iodine to bronchiectatic cavities through the bronchoscope as a therapeutic measure. Subsequent X-ray plates showed an outline of the cavities. In the same year Waters, Bayne-Jones, and Rowntree, in order to visualize the tracheo-bronchial tree in dogs, introduced a 10 per cent emulsion of chemically pure iodoform in olive oil. Because of a 25 per cent mortality in their animals, no clinical application was made of the use of iodoform intratracheally.

Weingartner, in 1919, insufflated the lungs of three patients with anhydrous thorium-oxydate. Lynah and Stewart, in 1920, introduced a bismuth subcarbonate suspension in olive oil through the bronchoscope into two lung abscesses, which they were able to visualize radiographically. In 1921 they reported five cases in which this diagnostic procedure had been used.

With the exception of these few isolated instances, bronchography was seldom used before the introduction of the iodized oil, lipiodol, by Sicard and Forestier, in 1922. They, together with Leroux, were the first to introduce iodized oil into the tracheo-bronchial tree. Since that time, bronchography has become a well recognized and

[1]From the Department of Surgery, Tulane University Medical School, New Orleans, Louisiana. Read before the Radiological Society of North America, at New Orleans, Dec. 1, 1927.

well established procedure. It is to the pulmonary system what the barium meal examination is to the gastro-intestinal system and the pyelogram to the genito-urinary system.

INDICATIONS FOR BRONCHOGRAPHY

In all chronic pulmonary affections in which the diagnosis is not clear a bronchography is indicated: it is of primary importance in diagnosing cases of bronchiectasis. The dilated bronchi become filled with the contrast substance, making a detection of the dilatation relatively easy. This is true, not only in the cases which are typically bronchiectasis clinically, but also in those which are merely suspected. Bronchography serves as a means of differentiation between bronchiectasis and lung abscess. The patient may give a history typical of pulmonary suppuration, but from the history and physical findings it may be impossible to determine just what type of suppuration he has. Even though it is, at times, very difficult to fill a pulmonary abscess with iodized oil, because of the small communication between the abscess and the bronchus, which is often so plugged with granulation tissue that the viscid oil cannot enter the cavity, a negative result in a patient with a history of a typical pulmonary suppuration leads one to make a diagnosis of pulmonary abscess. If a bronchiectasis were responsible for the condition, a typical radiographic picture of the filled dilated bronchi would be seen.

Because of the large number of cases of non-tuberculous bronchiectasis treated in tuberculosis sanatoria (Hamilton, 25 to 50 per cent, David Ballon, 50 per cent), a bronchography is especially useful in differentiating this disease from tuberculosis. It must not be forgotten, however, that a tuberculous bronchiectasis may occur. Most cases, nevertheless, in which a mistaken diagnosis is likely to be made, are those that have symptoms of a chronic pulmonary affection but in which tubercle bacilli have not been found.

Lenk, Haslinger, and Presser consider bronchography as one of the most useful methods which may be employed in diagnosing tumors of the bronchi. Strictures of the bronchi, whether they be benign or malignant, can be visualized following the introduction of the iodized oil into the tracheobronchial tree. Clerf employed a bronchography to show the relationship of a foreign body within the parenchyma of the lung to the bronchi. In this way it can be determined whether a foreign body within the parenchyma of the lung may be removed through the bronchoscope, or whether a thoracotomy will be necessary.

To the thoracic surgeon bronchography is indispensable, because it permits him to visualize the condition of the involved and uninvolved lung. Following the collapse of a lung, the degree of collapse may be ascertained by this method. This was first brought out by Archibald, and later emphasized by Lorey. Not infrequently patients, for whom a thoracoplasty has been done for pulmonary tuberculosis, do not recover as well as might be expected. The collapse, though clinically very satisfactory, is shown by the bronchography to be incomplete.

Bronchopleural fistulæ may also be demonstrated by a bronchography (Moeller and Magnus; Jacobæus; Escudero, Terrada, and Gallino; Pritchard, Whyte, and Gordon; Ballon).

As Forestier has brought out, a bronchography can be used to good advantage in cases following a therapeutic pneumothorax to determine whether an attachment of the lung is really lung tissue or merely a membrane. As in surgical collapse, a bronchography is a guide concerning the amount of collapse.

In addition to all of the above indications of bronchography, which are indeed very important, there remains a much more frequent indication, and, probably for this rea-

son, most important. All patients with a chronic cough lasting over two or three months should be given the advantage of a bronchography. These much-to-be-pitied individuals usually wander from doctor to doctor, and from each obtain a bottle of cough medicine. The so-called chronic bronchitis, however, persists in spite of all therapy. Over 90 per cent of these individuals are suffering from bronchiectasis, which can easily be demonstrated following an introduction of a contrast substance into the tracheo-bronchial tree.

Irrespective of the type of procedure employed to introduce the contrast medium into the tracheo-bronchial tree, it is absolutely imperative to observe the case fluoroscopically, and it is also important to observe the tracheo-bronchial tree during the introduction of the oil, so that the mode of filling of the bronchi may be noted. X-ray plates should be used only for confirmation and record. Because the iodized oil may be aspirated into the alveoli within a very short period of time after the introduction of the oil, a haziness of the lung field is obtained, due to the presence of the oil in the alveoli. This very commonly obscures the outline of the bronchi, so that a dilatation may be overlooked. On four different occasions I have been able to make a diagnosis of definite bronchiectasis during the introduction of the oil into the tracheo-bronchial tree, while the roentgenograms, taken immediately after the fluoroscopic examination, showed the presence of the oil in the alveoli, producing such haziness that it was impossible to say whether there was a dilatation of the bronchi or not. One especially instructive case has been described in detail in a previous publication, but, as it so aptly illustrates the point under discussion, I will give a brief résumé of its history.

An adult male, who, during the influenza epidemic, had influenza followed by an empyema, has since had symptoms very suggestive of a bronchiectasis. A bronchography, done according to the "passive" technic so that the mode of filling of the bronchi might be observed under the fluoroscopic screen, revealed definite, saccular, and cylindrical dilatations of the bronchi of the left lower lobe, the side involved by the empyema. In less than a minute's time, however, the iodized oil had gotten out into the alveoli, producing such a haziness of the pulmonary field that, had one seen the picture at this stage only, a diagnosis of bronchiectasis could not have been made. An X-ray plate taken at this time showed no evidence of bronchiectasis. The radiologist, in reading the plate, reported that there was no evidence of bronchial dilatation. This same procedure was repeated on three different occasions, and each time the radiologist, who had not been present at the fluoroscopic examination, refused to make a diagnosis of bronchiectasis. It was not until he, himself, had observed the mode of filling within the first thirty seconds after the introduction of the iodized oil, that he become convinced of the existence of a bronchial dilatation.

Grill and Danielsson and Manfred have also emphasized this possible source of error, and they, too, strongly advocate the fluoroscopic observation of the mode of filling of the tracheo-bronchial tree with the iodized oil.

Another error may be made if the radiograph is depended upon for a diagnosis. In the anterior-posterior view those bronchi located at the greatest distance from the plate will, because of their distance, appear larger and give a mistaken idea of bronchial dilatation. This possibility was first brought out by Sergent and Cottenot, and further emphasized by Lorey, Lenk and Haslinger, and Singer. This error may be easily obviated by a fluoroscopic examination, because, as in the ordinary gastro-intestinal fluoroscopy, the patient is not only observed in the anterior-posterior position, but is

turned in various directions. In this way, it would be impossible to have two parallel bronchi superimposed upon each other in such a manner as to give a false impression of a bronchial dilatation.

For the above reasons it is self-evident that not only should roentgenograms be taken immediately, but that it is imperative to examine the patient under the fluoroscopic screen during the introduction of oil. In spite of these very obvious reasons, Abramovitch advises waiting fifteen to thirty minutes after the introduction of the iodized oil before taking an X-ray plate. He gives no reason for this delay, and, judging from the plates which are reproduced, he evidently has none.

If the fluoroscopic observation is the all-important factor in making a correct diagnosis following the introduction of iodized oil into the tracheo-bronchial tree, it is self-evident that the roentgenologist is the one who should do bronchography. Unfortunately at the present time this is not the general state of affairs, because, I believe, over 75 per cent of the bronchographies which are done are carried out by either laryngologists, internists, or surgeons. Following the introduction of the iodized oil, a radiograph is taken and the responsibility shifted to the radiologist's shoulders.

If a bronchography is to be carried out in all the cases in which it is indicated, it is then essential to employ a technic which is not only easy to execute on the part of the physician, but is not unpleasant to the patient, and is not time-consuming. The simpler the technic and the fewer instruments employed, the more nearly ideal is the procedure.

METHODS EMPLOYED FOR INTRODUCING IODIZED OIL INTO THE TRACHEO-BRONCHIAL TREE

The various methods which have been used to introduce iodized oil into the tracheo-bronchial tree are, briefly, as follows:

1. *The transglottic.*—By means of a laryngeal cannula, which, following complete anesthetization of the pharynx and larynx, is introduced into the larynx. A syringe is then attached to the cannula, and the iodized oil is injected through the cannula into the trachea. This probably is the most widely used method at the present time.

2. *The subglottic, or intercricothyroid.*—This technic consists of inserting a needle through the cricothyroid membrane directly into the larynx, through which needle the oil is introduced into the trachea. While this method is preferred by such authorities as Armand-Delille and his co-workers, Besançon, Weil, Bernard, Azoulay, Hedblom, and Head, it is not without danger. The procedure, simple as it may seem, is nevertheless an operative procedure, and bad results have been reported following its use. Leroux and Bouchet report a fatal case, death being caused by a local infection following the introduction of the oil into the trachea by the intercricothyroid route.

3. *Intratracheal methods.*—Several different intratracheal technics have been developed by different observers. Beck and Sgalitzer and Lenk and Haslinger introduce the iodized oil into the trachea by means of a catheter inserted through the larynx into the trachea. In this way the oil may be injected while the patient is under the fluoroscopic screen. Lorey has modified this technic somewhat in that instead of employing a simple catheter he uses one with a small metal olive on the end of it, which remains in place. Wierig uses the Lorey catheter, but, instead of introducing it merely through the larynx into the trachea, places the metal olive in that primary bronchus which he wishes to fill, and believes that in this way he gets a much better filling of the tracheo-bronchial tree. In this country, Iglauer employs a modified intuba-

tion tube, inserted into the larynx, through which tube the oil is injected.

4. *The supraglottic method of Pritchard.*—This method consists of introducing the iodized oil into the hypopharynx, through a cannula, at the same time instructing the patient to breathe. A certain percentage of the oil is aspirated into the trachea and bronchi. This method has been described by Caussade and Tardieu, and Pritchard.

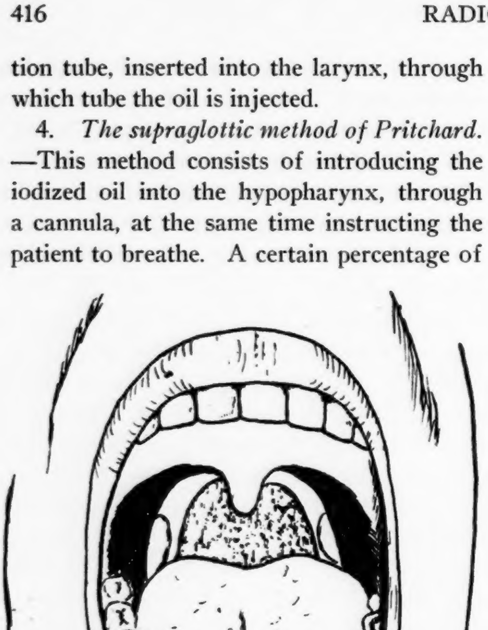

Fig. 1. Diagrammatic sketch showing area to be anesthetized with 10 per cent cocain. The shaded area represents the anterior tonsillar pillar.

5. In 1922 *Lian, Darbois and Navarre described a method of introducing substances into the trachea.* This technic consists of forcefully pulling the tongue out to such an extent that the patient cannot swallow. This technic has been popularized in America by Singer.

6. *Bronchoscopic method.*—Most of the bronchographists advocate the introduction of the iodized oil through the bronchoscope. This technic is especially advocated by Jackson, Clerf, Tucker, Ballon, Vincent, Hamilton, Kernan, Willy Meyer, and Pirie.

Iodized oil can be introduced into the tracheo-bronchial tree by any one of the above methods; still, each has the disadvantage of being more or less complicated and requiring a certain amount of skill, varying with the different procedures. All of them are more or less unpleasant for the patient.

As brought out before, a bronchography, in order to be useful, should be of such a nature as to be executed without the procedure's being unpleasant for the patient or difficult for the physician. The technic should be so simple that the roentgenologist, who is the one to do the bronchography and who usually has had no training in intralaryngeal manipulation, can carry it out without any difficulty. The "passive" technic of bronchography, which has been reported in detail in previous publications, fulfills all of these requirements. The technic is extremely simple and easy to carry out, requiring no special training nor special apparatus. The only instruments used are two sterile medicine glasses, several cotton applicators, and a tongue depressor. It is not at all unpleasant for the patient, as evidenced by the fact that in over a thousand fillings no patient has ever objected to a re-fill. As example of this, I wish to quote a letter received from a colleague:

"At variance with several articles appearing in medical journals, I have found in my own case that intra-bronchial use of lipiodol is attended with happy results and no unpleasant effects. My experience is that the so-called 'ordeal' is no more trying than shaving and no more dangerous than having one's hair trimmed. Having entered the bronchi, lipiodol immediately induces (locally) a sedative and soothing effect and relieves cough for at least two days. It is unfortunate that the use of this valuable treatment has been curtailed by unskillful methods."

In addition to these very important ad-

vantages of the "passive" technic, there is still another advantage, which, in my mind, is the most important of all, namely, the "passive" technic is the ideal procedure for introducing iodized oil into the trachea and bronchi because of the ease with which the mode of filling of the bronchi under the fluoroscopic screen may be observed. As has been brought out before, the fluoroscopic observation of the oil entering and filling the bronchi is much more valuable than an interpretation of the X-ray plate.

"PASSIVE" TECHNIC

After cleansing the mouth with an antiseptic mouth wash, the anterior surface of the anterior tonsillar pillar is swabbed with a 10 per cent cocain solution. The anesthetic solution is applied to the whole anterior pillar from the uvula to the angle between the anterior pillar and the tongue (Fig. 1). The anesthesia is continued until the swallowing reflex is abolished. As evidence that this has been accomplished, the mobility of the larynx during attempted deglutition is observed. As soon as the larynx remains immobile upon attempted deglutition, the anesthesia is complete. The patient is then given 3 to 4 c.c. of a 3 per cent novocain solution and instructed to tip the head backward, protrude the tongue, lean toward the affected side, and breathe (Fig. 2). The novocain solution is used for two reasons:

(1) In those cases where there is not a great deal of secretion, where the cough reflex is more or less normal, the novocain acts as an anesthetic to the tracheo-bronchial mucosa. Following this, the oil may be aspirated into the tracheo-bronchial tree without being coughed up.

(2) A patient who has been accustomed to carrying large amounts of secretion in his tracheo-bronchial tree has lost his normal cough reflex. This individual will be able to tolerate large amounts of fluid in the bronchial tree before a cough is produced. Coughing in these patients occurs only when the secretion becomes great enough to come in contact with the mucosa of the first primary divisions of the bronchi. Not infrequently, following the introduction of the oil, which may be just enough to fill the tracheo-bronchial tree up to the point where a cough reflex is instituted, the patient coughs and expectorates all of the oil. In this type of case, even through an anesthesia of the tracheo-bronchial tree is not necessary, a novocain solution acts as the oil would, filling the tracheo-bronchial tree to that point where a cough reflex is instituted, produces the cough, and thus causes an evacuation of the secretion of the tracheobronchial tree. This leaves the bronchi comparatively empty so that they may be filled with the iodized oil.

Following this procedure, the anterior pillars are again painted with 10 per cent cocain and the patient placed behind the fluoroscopic screen. The effect of the application of cocain to the anterior pillar is only temporary, usually lasting from one to two minutes. It is, therefore, imperative to make an application just previous to the placing of the patient behind the fluoroscopic screen. While under the screen the patient is instructed to take 10 c.c. of the iodized oil into his mouth and aspirate it into the tracheobronchial tree in the same way in which the novocain solution was aspirated (Fig. 2). By means of the fluoroscope, the oil is seen to enter the larynx, fill the pyriform sinus of the larynx on each side, pass through the trachea, and into the bronchus. The lobe filled depends upon the side toward which the patient is leaning, *i.e.*, if the patient leans to the right the right lower lobe fills, and *vice versa*. The patient is then turned in various directions, in order to rule out any apparent dilatation caused by the bronchi's being located a greater distance from

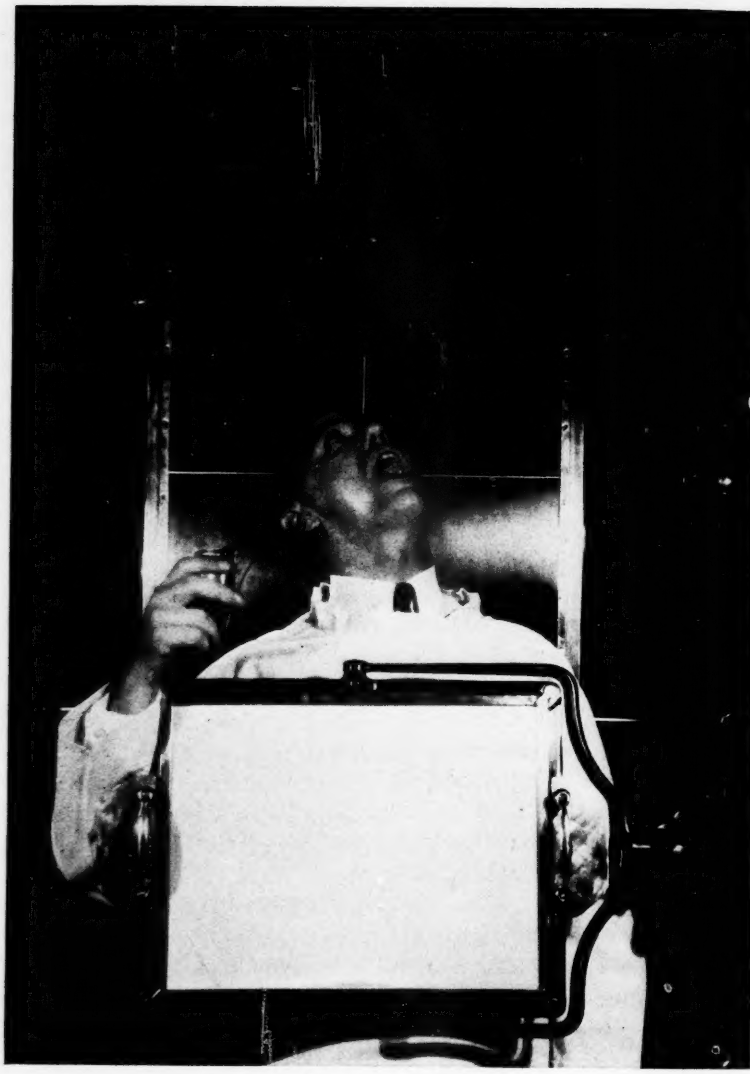

Fig. 2. Attitude assumed by the patient in aspirating the contrast substance into the tracheo-bronchial tree. The head is tipped back, the tongue is protruded, and the patient is instructed to breathe naturally.

the screen. Any deviations from the normal bronchi, either in course or contour, are carefully noted. A diagnosis should always be made from the fluoroscopic observation. After the 10 c.c. of oil has been aspirated, the patient is instructed to expectorate the saliva which has accumulated in the mouth and to take another 10 c.c. of oil and aspirate it in the same manner. After the 20 c.c. of oil has entered the bronchi a roentgenogram may be taken for confirmation or record.

In order to understand the mechanism by which a "passive" bronchography is possible,

it is essential to recall some points concerning the physiology of swallowing. Swallowing is divided into two phases—a voluntary and an involuntary phase. The voluntary phase consists of masticating the food, the upper esophageal orifice, which, as Killian has brought out, is normally tonically contracted as is the cardia, and becomes relaxed only when an inhibitory impulse is supplied it. There is also an elevation of

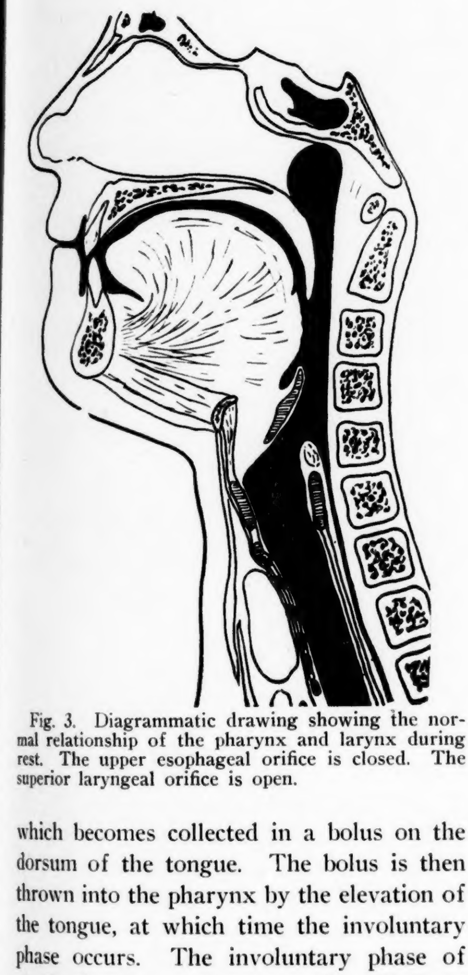

Fig. 3. Diagrammatic drawing showing the normal relationship of the pharynx and larynx during rest. The upper esophageal orifice is closed. The superior laryngeal orifice is open.

Fig. 4. Diagrammatic drawing illustrating the position of the larynx during deglutition. The larynx has moved upward to a position between the epiglottis and the base of the tongue. The superior esophageal orifice is released and open.

which becomes collected in a bolus on the dorsum of the tongue. The bolus is then thrown into the pharynx by the elevation of the tongue, at which time the involuntary phase occurs. The involuntary phase of swallowing is a reflex act. Wassilieff, in 1887, found that the swallowing reflex could be instituted by irritating or stimulating the mucosa on the anterior surface of the soft palate from the center of the tonsillar region up to the hard palate. An anesthesia of this area abolished the swallowing reflex. Immediately following the institution of the swallowing reflex, there is a relaxation of

the larynx to a safe position beneath the base of the tongue and the epiglottis. At the same time there is a contraction of the pharyngeal muscles (Figs. 3 and 4). If a sensory anesthesia is produced at that point where the swallowing reflex is instituted, none of the acts occurring normally in swallowing result. There is no contraction of the pharyngeal muscles, there is no elevation of the larynx to a point of safety beneath the base of the tongue and epiglottis, and there is no relaxation of the upper

esophageal orifice. Any food or substance taken into the pharynx at this time cannot enter the esophagus, but can enter the only one remaining opening—the larynx. If iodized oil is introduced into the pharynx, it is immediately aspirated into the trachea and bronchi.

The advantages of the "passive" technic become self-evident. Because of its simplicity it can be carried out by one who has not had special training in intra-laryngeal manipulation. As the oil is introduced into the tracheo-bronchial tree without any effort on the part of the physician, a fluoroscopic examination may be easily, and should be, made during the introduction of the oil in every case. The procedure, because of its simplicity and lack of instrumentation, is not unpleasant to the patient, and, therefore, the ideal procedure.

SUMMARY

1. A bronchography is an extremely useful diagnostic procedure; the indications for its use are many.

2. The fluoroscopic observation of the mode of filling of the tracheo-bronchial tree with the iodized oil is by far more important from a diagnostic standpoint than the interpretation of the X-ray plate.

3. Because of the necessity of fluoroscopic observation a bronchography should be done by the roentgenologist.

4. In order that a bronchography may be done in all indicated cases, it is necessary to introduce the contrast substance into the tracheo-bronchial tree by a method which is most simple to execute and easy for the patient, and also permits the fluoroscopic observation of the mode of filling of the trachea and bronchi.

5. Of the various methods of bronchography advocated up to the present time, the "passive" technic fulfills these requirements best. For that reason, it is the method of choice, especially for the roentgenologist.

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DISCUSSION

Dr. Jacques Forestier (Aix-les-Bains, France): I feel much interested in being asked to discuss Dr. Ochsner's paper, because it seems to me remarkable that a professor of surgery has been so keenly interested in a method which seems, at first, essentially medical. Prof. Ochsner should be greatly praised for it, because he is demonstrating that specialization in medicine does not always restrict the action of the physician, but on occasion allows him some interest in other fields of science.

I wish to make two points on this very particular technic that he has described—it is to me very interesting. I know it only through reading abstracts of his papers, but it appeals to me on account of its simplicity. It also allows for the possibility of fluoroscopy during the injection, a point on which I entirely agree. I must say that if it were not for the dangers of prolonged fluoroscopy, this should be adopted as a general method and any X-ray diagnosis should be arrived at by combining fluoroscopy and radiography. There is another point on which I agree with Dr. Ochsner—his producing some degree of local anesthesia of the bronchial tree before giving his patient lipiodol. It is a small point of technic which is rather important, because most of the failures which we encountered at the beginning of our experience in bronchography came about because we did not know how to suppress the cough reflex. I am sure that when this "passive" technic is properly carried out, one should succeed in getting the lipiodol into the bronchial tree quite well. Of course, there are a few objections which may be offered. First, there is the fear of bringing down through the natural passages such infective material as may have been gathered in the mouth or on the teeth or tonsils. I think that a previous careful examination of the patient's mouth may avoid all accidents of this sort, for, if such infective material is found, another method, especially the cricothyroid, may be employed. There is a second objection. I do not believe, from the pictures which have been shown here and from my experience with bronchography, that such a method affords a good visualization of the apices. When you ask a patient to bring the lipiodol into the bronchial tree, he must be in the erect position. Reversely, if we wish to

visualize the apices, we know that the patient must be in a recumbent position. But I believe it is possible to improve this method and perform the visualization of the apices after some small modifications. Last, I want to say that one particular feature of this method appeals to me: that it may be repeatedly used for therapeutic action. As Dr. Ochsner has pointed out, the therapeutic value of lipiodol may be still open to discussion, but there is a possibility of this action, whatever mechanism may be offered for an explanation. Thus, such a simple method, which allows a good introduction of the oil into the bronchial tree in most cases, is important to the chest man in the way of improvement in treatment. I am much indebted to Dr. Ochsner for the new field which he has opened up here for the use of lipiodol, both in radiodiagnosis and in the treatment of chest diseases.

Dr. Ochsner (closing): There is just one point, brought out by Dr. Forestier, that I would like to emphasize. It has to do with the method we use in getting the oil into the upper lobes. While it is more difficult, still it is quite simple. The patient is seated under the fluoroscope, and, as soon as the oil is seen to enter the trachea, he is tipped over so that the shoulders are lower than the pelvis and the oil runs in by gravity. In this way we have been able to handle several cases in which we suspected lesions in the upper lobe. However, it is not so satisfactory because we cannot observe fluoroscopically, but it is possible to get a plate. For the lower lobe the procedure is simple.

In regard to Dr. Forestier's statement concerning therapeusis, I do not think there is any doubt but that lipiodol has a distinct therapeutic value. In many cases we have been able to prove positively that the number of organisms in the sputum has been decreased following the introduction of iodized oil—decreased not only in the number of organisms, but the cases have become absolutely symptom-free. The patients still have cavitation and are subject to reinfection. I do feel, however, that in these early cases we can expect to get an ultimate cure, provided we get them early enough.

SOME PHYSICAL PROPERTIES OF FLUORESCENT SCREENS[1]

By FRANK E. SWINDELLS, PH.D.,
Research Chemist, the Patterson Screen Co., TOWANDA, PENNSYLVANIA

THE property of fluorescence in a substance is its ability to emit radiation of one quality when stimulated by radiation of another quality. A familiar example of fluorescence is the luminous paint used on the dials of watches and other instruments to render them visible in the dark. The fluorescent body is a sulphid of zinc or some other metal. It transforms the invisible radiation of the trace of radio-active material present in the paint into visible radiation or ordinary light.

Closely allied to fluorescence is the phenomenon of phosphorescence. In a fluorescent substance the transformation of energy takes place almost instantaneously, whereas a phosphorescent substance continues to emit radiation for an appreciable time after the stimulating radiation has ceased. An excellent example of a phosphorescent material is an intensifying screen showing lag, about which more will be said later.

Probably the most extensive application of the phenomenon of fluorescence is in the fluoroscopic and intensifying screens which every radiologist and technician uses daily. The use of fluorescent substances in X-ray work dates from the discovery of X-rays in 1895, for it was by means of a fluorescent screen of barium platino-cyanide that they were discovered by Roentgen. The sudden shining of a fluorescent screen in a darkened room in which X-rays were being generated, unknown to this experimenter, led to one of the greatest discoveries of modern times.

It was soon appreciated by the early workers who attempted to take radiographs that only a small part of the energy of the rays was utilized by the photographic plate, for the bulk of the energy passed through unabsorbed. In order to make use of a part of this waste energy, the first intensifying screen was devised. In this case a considerable proportion of the energy of the X-ray beam is absorbed by the screen and by means of its fluorescence is converted into actinic or ordinary photographically effective light. This light adds its effect on the plate to the effect caused directly by the X-rays, thereby reducing several fold the exposure required to produce a given blackening of the plate. The present form of the double screen used in conjunction with a photographic film coated on both sides is a further development of the same idea.

The earliest intensifying screens used calcium tungstate as the active fluorescent material and this chemical is still used in practically all makes of intensifying screens. Nevertheless, the first screens were quite crude compared to the present-day product. They were very fragile, easily soiled and scratched, and not capable of being cleaned. The layer of active material was subject to many irregularities and imperfections, and if two screens had the same speed it was only a coincidence. Most of the early screens had the extremely objectionable features of grain and lag or afterglow. They frequently produced a mottled effect over the entire radiograph which obscured most of the fine detail. In spite of the many defects, intensifying screens were quite widely used because they were the only means available for reducing the unusually long exposures of early radiography.

The development of intensifying screens to their present high state of perfection has taken place mainly along two lines: improvements in the manufacture of fluorescent calcium tungstate and in the fabrication of the screens. As a result of extensive re-

[1]Presented before the American Association of Radiological Technicians at the Third Annual Meeting, Chicago, April 24, 1928.

search on the part of some of the screen manufacturers it is now possible to produce calcium tungstate of absolute uniformity of fluorescent properties and physical state, which, with modern methods of manufacture and rigid inspection of the finished screens, produces screens of such high quality that their employment actually adds to the quality of the radiograph in most cases.

It was stated previously that the evolution of the modern intensifying screen took place through the development of manufacturing methods rather than by the discovery of new fluorescent materials. At the present state of our knowledge calcium tungstate, properly prepared, is by far the most suitable chemical for this purpose. It may be interesting to you to know that the fluorescent power of calcium tungstate is intimately associated with the development of its crystalline state. Amorphous calcium tungstate, prepared by precipitation under the proper conditions, is absolutely non-fluorescent. It has been shown that as the conditions of preparation are changed to give larger percentages of the crystalline state, as shown by X-ray diffraction photographs, the fluorescent power develops proportionally, and is at a maximum when the salt is all in the crystalline state.[2]

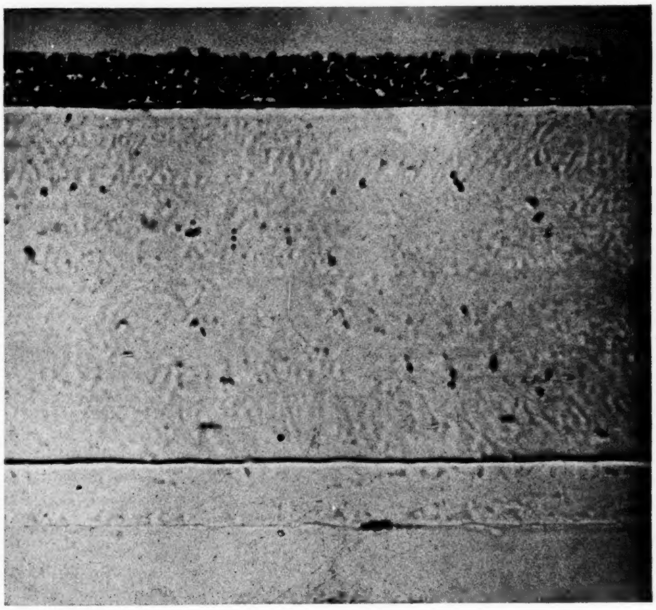

Fig. 1. Cross-section of film exposed directly to X-ray beam.

A further examination into the mechanism of the intensification process will show why calcium tungstate is peculiarly adapted for use in intensifying screens. When a radiograph is taken, a small portion of the X-rays is absorbed by and acts on the photographic film directly, but the greater part is absorbed by the screens and is transformed into ordinary light, which also acts on the film. In this connection it is interesting to compare the action of X-rays and light on an X-ray film. Figure 1 shows a microphotograph of a section cut through a film exposed to X-rays sufficiently long

[2]Tiede and Schleede, Ztschr. für Electrochemie, 1923, p. 304.

to produce a moderate density. It will be noted that the black spots, which are exposed and developed silver halide grains, actually much darker to the eye, will photograph as white. The colors which are most efficiently photographed are in the violet end

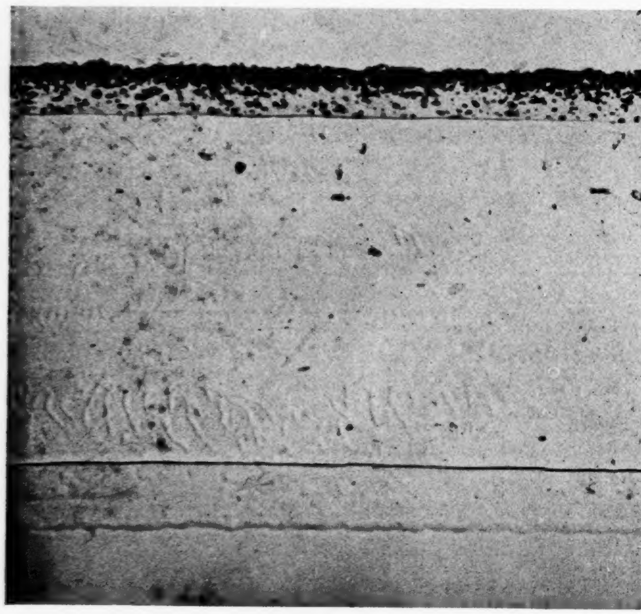

Fig. 2. Cross-section of film exposed to X-rays by medium of intensifying screen, having same density as shown in Figure 1.

are uniformly distributed throughout the photographic emulsion layer. In Figure 2 is shown a similar section cut through a film exposed and developed to the same density by the medium of a screen. Here we note that the large part of the exposure has taken place at the surface of the film, showing that the larger part of the exposure is due to fluorescent light from the screens, which is readily absorbed at the surface of the emulsion, and the comparatively small amount of exposure in the deeper part of the emulsion layer indicates the relative unimportance of the direct effect of the X-rays.

It is no doubt known to all of you who are outdoor photographers that certain colors are more effectively photographed than others. Thus a bright red will photograph as black, but a blue or violet, which appears of the spectrum and extend into the invisible ultra-violet. The region of greatest color sensitivity of an ordinary X-ray film is found to be in the violet and near ultraviolet regions of the spectrum (3,800 to 5,200 Å.U.).[3] The light emitted by the intensifying screen is confined almost entirely to this region.[4] Thus with a calcium tungstate screen the fluorescent light is all utilized to the best advantage with present-day photographic materials.

I will at this point digress from the general subject of intensifying screens to show similar curves for a fluoroscopic screen of good quality. In the case of a fluoroscopic

[3]From data supplied by the courtesy of the Agfa Ansco Corporation research laboratory.

[4]P. Schuknecht, Ann. Physik., 1915, XVII, 717; M. B. Hodgson, Phys. Rev., 1918, XII (2), 431; J. O. Perrine, Phys. Rev., 1923, XXII (2), 48, and unpublished measurements of the author.

screen we are not interested in actinic power but in visual intensity. In other words, instead of making a screen whose fluorescent light is of a color most readily photographed, we attempt to make a screen whose color is most readily perceived by the human eye.

It has been found that the average human eye, when well accommodated to feeble light, gives the greatest response to light of about 5,100 Å.U.[5] Naturally this value will vary somewhat with different individuals, but the value given is obtained by averaging the results from a number of persons. An examination of the light emitted by a high quality fluoroscopic screen shows that most of this light lies in the region from 4,300 Å.U. to 5,400 Å.U. Thus it will be seen immediately that for the color region where the eye is most sensitive the fluoroscopic screen is most brilliant.[6]

Returning to the subject of intensifying screens, we will next consider briefly the subject of lag. By lag or afterglow is meant the property which some screens have of continuing to emit light after the X-ray stimulus has ceased. This may cause embarrassment to the radiographer if the cassette is reloaded before the lag has disappeared, for a more or less complete image of the preceding radiograph will be formed on the fresh film which he believes to be unexposed. A more frequent source of annoyance from screens having lag is that in the handling of cassettes containing exposed films even a slight jar may displace the film relative to the screens, and thus produce a blurred image.

Under ordinary conditions it is difficult to detect any lag in modern intensifying screens of good quality, but occasionally a screen with considerable lag is encountered. Screens have been recently described in which the lag has persisted for as long a period as three months after the exposure to X-rays.[7] The writer has made a study of lag in screens, using for the work a screen specially prepared to have considerable lag.[8]

Some of the conclusions which may be of interest will be repeated here.

First, the intensity of the lag or phosphorescent light is proportional to the exposure up to a certain limiting value. That is, if an exposure of 30 milliampere-seconds produces an afterglow of a certain intensity, an exposure of 60 milliampere-seconds at the same voltage, distance, etc., and with the same screen, will produce an afterglow of twice the intensity of the preceding case.

Second, above the limiting value of the exposure, increased exposure produces no increase in the lag. That is, exposures of 2,000 or 5,000 or 10,000 milliampere-seconds at the same voltage would produce exactly the same lag, if these exposures were all above the saturation point.

These results are of some theoretical interest. A widely accepted theory of phosphorescence states that in phosphorescent compounds there are located unstable "centers of phosphorescence." As the X-ray stimulus is applied, a change takes place in the centers; they become excited or activated. When the activating effect of the X-rays is removed, the centers gradually return to the unexcited state, some immediately, and some after various time-intervals have elapsed. This process of the return of the centers to the unexcited state gives rise to light which appears as the phosphorescent afterglow. This light is at any time proportional to the number of centers which were originally excited, which, in turn, is proportional to the X-ray exposure. As the X-ray stimulus is increased, more

[5]Hecht and Williams, Jour. Gen. Physiology of the Rockefeller Inst. Med. Res., 1922-3, V, 1.

[6]P. Stumpf, Fortschr. auf dem Geb. der Röntgenstrahlen, 1925, XXXIII, 731, and unpublished measurements of the author.

[7]G. L. Clark, "Applied X-Rays," McGraw-Hill Publishing Co., 1927, p. 76.

[8]Jour. Opt. Soc. Am. and Rev. Sci. Inst., 1928, XVI, 165.

and more centers become excited, until a point is reached where all the centers are excited, and thus a further increase in the exposure does not increase the phosphorescence.

The emission of the phosphorescent energy may be accelerated by heat, but in that case its duration will be less, since the total energy emitted must be the same regardless of the temperature. If a phosphorescing screen be warmed even slightly, a noticeable increase in the phosphorescent glow will take place, and if it be considerably warmed, it will light up quite brightly for a moment, after which the glow will disappear entirely.

Next we will consider a few of the factors which may influence the speed of intensifying screens. The determining factor in the speed of a screen is its ability to emit fluorescent light of the proper actinic power. The fluorescent light is, of course, proportional to the intensity of the X-rays striking the screen, provided the quality of the rays does not vary. It is quite probable that a saturation value is reached similar to that found for phosphorescence, but this value is probably considerably beyond the limits of practical radiographic exposure.

The intensification factor, or the factor by which an exposure with screens must be multiplied to get an equivalent exposure without screens, is a function of several variables. It is to be expected that it will vary from screen to screen, dependent on the make of screen and the care exercised in its use. But it is not a constant for a given pair of screens, but is dependent upon the conditions under which the screens are used. It has been shown to vary widely with the hardness of the radiation, having its lowest value for the rays of greatest wave length, or soft X-rays.[9] Thus, at rather low voltages the intensification factor in much lower than at high voltages, where the beam contains a greater proportion of hard rays. Also, where deep parts of the body are being radiographed, the composition of the beam of X-rays striking the cassette may be quite different from that of the original beam, and its effective wave length increased due to the presence of secondary radiation. The net result is that the intensification factor is appreciably less than if the original beam had been permitted to strike the cassette.[10] The intensification factor should not be confused with the absolute amount of blackening or photographic density. It is, as previously stated, the ratio of the two exposures, one with screens, the other without, necessary to produce equal blackenings in the two radiographs, taken otherwise under identical conditions.

Furthermore, the intensification factor is not a constant throughout the range of densities on a single radiograph. It is least on the lightest parts of the radiograph, increases at the moderate densities, and falls off slightly when the densest parts of the radiograph are reached. The underlying cause for this variation is rather obscure, and it will suffice to say here that it lies in the fundamental difference in the action of X-rays and light on a photographic emulsion.[11] In this connection we also notice some variation of the intensification factor with different makes of film. This difference is obviously explained by the different relative speeds of the films to X-rays and light.

In summarizing, it may be stated that the intensifying action, or the efficiency of intensifying screens in practical use, depends upon: first, the quality of the radiation as affected by the voltage, filtering medium and secondary radiation photographed; second, the density of the radiograph, and third, the film or other photographic medium used.

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[9] W. de Broglie, Compt. Rendu., 1920, CLXXVII, 849.

[10] R. B. Wilsey, Radiology, 1924, II, 311.

[11] F. E. Swindells, Am. Jour. Roentgenol. and Rad. Ther., 1927, XVII, 115.

CASE REPORT

PREGNANCY COMPLICATED BY CARCINOMA OF THE UTERINE CERVIX

CASE REPORT

By WILLIAM NEILL, Jr., M.D., Baltimore

A therapeutic abortion by X-ray radiation is declared possible any time before the fifth month of pregnancy and even later if the treatment is properly administered.[1] In Stern's report the time of expulsion varied in most cases from 14 to 42 days, with one after 76 and another after 128 days. The age ranged from 19 to 40 years. Menstruation had not returned over periods of from 9 months to 2 years. Bowman[2] cites a patient treated with X-ray at the third month of pregnancy under a mistaken diagnosis of fibroid uterus, who went on to the delivery of a normal child at the eighth month. Martin[3] reports an instance, strikingly similar to the one I am about to relate, of a pregnancy with carcinoma of the cervix which was allowed to proceed to delivery by the induction of labor at the eighth month, after treatment with radium and X-ray during the second month, and the child was normal. The present condition of the cervix is not stated.

I report as follows:

A young colored woman presenting: (1) Carcinoma of the cervix clinically cured with radium; (2) complication of pregnancy; (3) delivery of a normal child by a Caesarean operation during the eighth month.

December 1, 1926, at my surgical clinic at the Cambridge Maryland Hospital, I was asked to see a colored woman, aged 28, with the complaint of irregular vaginal bleeding, with pregnancy. Her past history was negative as to serious illnesses or operations. She had been married ten years and had had four normal pregnancies. Her children were living, 3, 4, 7, and 9 years old, respectively. Normal menstruation began eight months after the birth of the last child and continued regularly up to June, 1926, when she became pregnant. In September she had some scanty vaginal bleeding, which had become more profuse at the time I saw her. Treatment had been given for threatened abortion, with bromides and rest in bed, without affecting the bleeding. There was never any pain nor were there uterine cramps; the health continued good and she gained in weight as the pregnancy advanced. She looked healthy and the general examination was negative. In her seventh month of a normal pregnancy the pelvic measurements were within normal limits, the fetal heart sounds clear and movements active. The pelvic floor was considerably relaxed and the vaginal wall normal. On the right

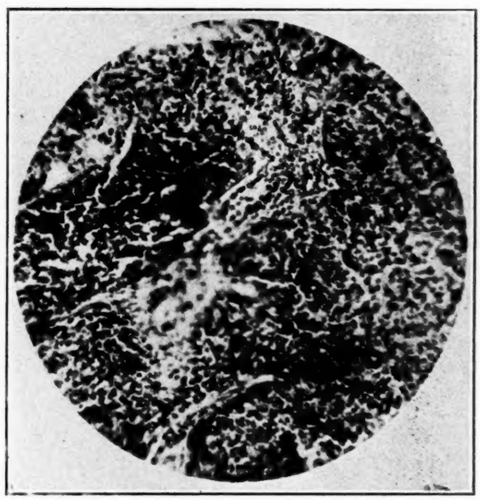

Fig. 1. Low power microphotograph of tissue from cervix, removed at operation, showing clusters of carcinomatous cells.

1S. Stern, Am. Jour. Roentgenol, and Rad. Ther., February, 1928, XIX, 133.
2Ibid.
3Ibid.

side of the cervix was a solid, indurated, non-ulcerating, rounded tumor a little larger than a golf ball, with its base involving the entire right half. The mucosa was hyperemic and bled on touch. The mass was movable, with cervix and fundus and fornices clear. There was no palpable disease in the lateral structures. The tumor, with the cervix, could be delivered entirely outside the vaginal orifice.

Diagnosis: Malignant growth limited entirely to the cervix.

Operation: Complete removal of the cervix. Pathological picture that of a squamous cell carcinoma (see Fig. 1).

December 15, 1926, four glass radium emanation seeds, each 2½ millicuries, were implanted permanently into the cervical stump, and December 18, 1926, 1,765 millicurie hours radium radiation was given direct. The pregnancy continued its normal course, with a cessation of the bleeding, until January 16, 1927, when her first labor pains began and a healthy female infant weighing 6 pounds 4 ounces (3,000 gms.) was delivered by Caesarean section. April 1, 1927, a superficial metastatic nodule 1 cm. in diameter was removed from the right vaginal orifice with the cautery. In September, 1927, both mother and child were well. At the time of making this report (April, 1928) the mother is well and there is no trace of recurrence. Menstruation has not returned. The child is healthy and developing normally in every way.

EDITORIAL

"ELECTRICITY IS DANGEROUS"

Some weeks ago, two physicians using X-ray equipment as an aid in diagnosis were killed.

The exact condition of the equipment at the time of the accident has not been learned. The fact, however, that these men were killed, makes a warning at this time apropos.

Immediately following the death of one of the physicians, a leading newspaper of the city in which the doctor resided carried a headline in bold type, "Doctor is killed by X-ray." That there are many men killed each year while working with electricity throughout the country is a known and accepted fact. Very few of these accidents call for headlines in our large daily newspapers. That these accidents are not featured is probably due to the fact that they are not spectacular and do not constitute so-called news. In other words, they do not cause any great amount of concern to the reading public.

Those familiar with the X-ray know quite well that these unfortunate doctors were not killed by the X-ray. X-rays do not cause death in such a short time or in such a manner. These men were killed by electricity, probably high-tension electricity, which becomes X-rays only when given off by the anode of the X-ray tube.

It is probably appropriate at this time to sound a warning to all those working with electrical apparatus: this applies especially to those using the apparatus as an adjunct in their daily practice of medicine. It is imperative that anyone using electrical apparatus, either for diagnostic or therapeutic purposes, be thoroughly trained in the use of such apparatus. Electricity is always potent and must be considered dangerous at all times. It is not sufficient that the physician shall obtain a smattering of information from some salesman. It is just as important for the protection of the public and himself that he shall prepare himself in the same sense as a specialist in any other of the various branches of medicine prepares himself.

High-tension current cannot be made absolutely safe. It can be and usually is safe if the ordinary amount of precaution is used. If plenty of space is not allowed between the wires or aërial and the patient, serious results will follow. There is no way that the installation can be made so-called "fool proof." If one forgets and gets too close to the circuit, an electrical shock will follow and death may result.

It is important that we, as Directors of Radiological Departments, school our associates in the importance of being careful—that each patient be given all protection possible. Look and think before doing. Regard electricity as a highly potent drug whose lethal dose is oftentimes very small.

E. L. Jenkinson, M.D.

THE COMMERCIAL EXHIBIT

Dr. I. S. Trostler reports that four-fifths of the space allotted to the Commercial Exhibit for the Fourteenth Annual Meeting,

to be held Dec. 3 to 7, inclusive, at the Drake Hotel, Chicago, was sold the first day it was offered. On the first of October only three spaces remained to be sold.

ADDRESS BY PRESIDENT-ELECT GRAY BEFORE THE AMERICAN COLLEGE OF RADIOLOGY, MINNEAPOLIS, JUNE, 1928

Mr. President and Fellows of the American College of Radiology: It is with a feeling of trepidation that I enter upon my duties as President of this College, realizing as I do how wholly incompetent I am to conform to the standards set by my predecessors and with full knowledge that the only qualification that I possess for this, the greatest honor that can be bestowed by American roentgenologists, is that I possess among you some very warm friends, who are, by reason of that friendship, willing to overlook my shortcomings in order to demonstrate that friendship. To you, therefore, I am doubly grateful for the honor that you have conferred upon me.

Would it were in my power to inaugurate some movement for the furtherance of our specialty that would be continued through the ages, as some small addition to our ability and preparedness to benefit mankind. My powers of inauguration are quite limited, far more so than my willingness to put into execution the plans and propositions of others.

In casting about me for some suggestion that I may offer, several questions of greater or less importance have occurred to me. You will recall that at our meeting in Washington last year there was brought up the question of insurance—both life and professional liability insurance. So far as I have been informed no definite action has been taken and the matter still remains in an unsettled state. The life insurance companies have in the past few years become stampeded by fatalities that have occurred as a result of exposure when we knew little of the effects of the roentgen rays or of radium rays and far less of adequate protection. It is, of course, folly to condemn the present generation for the ignorance of our pioneers, when modern methods of protection render the art of radiology far less a menace than confronts the surgeon with the dangers of inoculation or the medical man in his daily contact with the grave systemic infections. There should be set some criterion by which the insurance companies may determine whether or not a roentgenologist is working under proper protection, and be enabled to differentiate carefully between those who are properly protected and those working in haphazard, unsafe surroundings. Especially is this true in regard to professional liability insurance. A well trained specialist should not be made to suffer for the indiscreet and foolhardy methods pursued by those who, for financial or other reasons, enter the field of radiology without knowledge other than is given by the manufacturer's agent who installed the machine or sold the radium. Steps have been taken by the American Roentgen Ray Society which are being considered by the United States Bureau of Standards looking toward the protection of operator and patient. The adoption of these or some other standards would serve as a guide for the life insurance companies, while membership in one or more of our American societies maintaining high standards for admission might be adopted as a guide in issuing liability insurance.

One of the serious problems confronting the specialty of radiology and seriously affecting public welfare is the fact that there is a growing tendency to the establishment by non-medical operators of so-called labo-

ratories for diagnosis and treatment. Little less dangerous is the practice which obtains with fair generality in small community hospitals of securing a technician and leaving to the physician or surgeon in charge of the case the matter of diagnosis or treatment. To meet the former, my own state has recently revised its Medical Practice Act, which, having been passed by our last legislature, is now in effect. This act provides a penalty for diagnosing or treating disease for compensation by anyone who has not conformed to the requirements of the State Board of Medical Examiners enacted for practitioners of medicine. The clause covering this was specifically directed to the breaking up of non-medical radiological offices and departments and the prevention of the establishment of others. The second of these problems is one much more difficult to combat, and I know of no means of remedying it except by discouraging the general men on account of the dangers which confront them and the necessary inaccuracy of diagnosis and treatment that must of necessity obtain in the absence of special training in radiology.[1]

Recently there have appeared folders and advertisements in medical journals, some of which have been issued by what have been considered reliable and well established manufacturers, intended for the general office practitioner and leading to the belief that the possession of an equipment such as this manufacturer puts out is all that is necessary to bring to him great financial returns. One contains this expression: "Doctor, you too may have an X-ray machine in your office." Another manufacturer gives us this: "Every physician and surgeon has an abundance of use for the X-ray without encroaching upon the field of the X-ray specialist. Invaluable for examining the lungs, heart, gastro-intestinal tract, extremities, for bone pathology, reduction of fractures, and localizing of foreign bodies." What, pray, is left for the poor X-ray specialist to consider his field? Still another in a general medical journal presents a catchy heading thus: *"An Unusual Opportunity.* An essential part of the equipment of the modern office is an X-ray fluoroscopic unit. As a means of making and confirming diagnoses it is invaluable. It adds enormously to the prestige of the physician and brings him a dominating position in his community." Should we not take some steps to prevent this kind of propaganda? Do not these advertisements show on their faces that their main object is to sell the product of these manufacturers, without due regard for the consequences?

In the short period of the service that I may render as president of this College it will be my endeavor, with the approval of the College, to take such steps as are in my power to accomplish some of the ends that I have indicated. The first of these, as a member of the committee of our state medical society to revise the Medical Practice Act, I have already initiated by having urged the insertion in this act of the clause intended to prevent the use of X-rays for medical and surgical purposes by those unqualified to employ them.

Finally, whatever seems good for the advancement of the science and art of radiology will find in me an ardent supporter and an untiring advocate. Let me especially urge you to give me the benefit of your suggestions and help, since the endorsement by this College of any movement carries with it such force as may be put forward only by the world's established leaders.

A. L. Gray, M.D.

300 Medical Arts Building
Richmond, Va.

[1]Since presenting the foregoing paper I have been informed of the death by electrocution in the past few months of two physicians, not trained roentgenologists, in the city of Cleveland, Ohio, from lack of knowledge of the dangers in handling small office machines.

SPEECH DELIVERED AT THE OPENING OF THE SECOND INTERNATIONAL RADIOLOGICAL CONGRESS AT STOCKHOLM, JULY 24, 1928

BY THE PRESIDENT OF THE CONGRESS
PROF. DR. GÖSTA FORSSELL

From every corner of the world there is gathered here this day a host of scientists within the sphere of medicine, numbering approximately one thousand. It must be a strong and great force which has been able to gather together in Ultima Thule from their daily labor in the service of research so many men of science and industrious servants of humanity.

That which has united us here is also one of the most significant forces of life: Light.

Light is the source of energy for all living beings upon the earth, and through the organ especially created by Nature for our conception of light, the eye, we gain our knowledge of shape and color and movement in nature. Just as light is a *sine qua non* for life upon the earth, so has it also from time immemorial been used for elevating and strengthening the force of the entire organism. But as a conscientiously and properly used healing agent, to exercise direct influence upon local disease processes, light has not been harnessed to the service of medicine until the last few decades. This was done through Nils R. Finsen's introduction of the artificial, local light treatment. The great advance of light in therapeutics occurred, however, through Roentgen's discovery of the light bearing his name, the roentgen ray, and after Becquerel's discovery of radiating matter and the discovery by the scientists, the Curies, of the fundamental substance—radium.

In our day radiotherapeutics has acquired such an important position in medicine that one is undoubtedly justified in saying that it is one of the greatest new gifts which our age has presented to medicine. I need not, in this gathering, point out the different diseases in which radiotherapeutics has been employed in a form of roentgen treatment, radium treatment, or sunlight treatment. What has imparted to radiotherapeutics its general, and, in so many spheres, far-reaching importance, is the circumstance and the fact that radiation is capable of supplying the organism with a contribution of energy in its struggle against the morbid process. Through radiation upon the morbidly changed tissues the disease process is enfeebled, and the normal healing or recuperative forces of the body strengthened, or fresh healing and recuperative powers are produced in the same. This healing influence occurs in such widely different processes as inflammatory conditions of disease, in tuberculosis, in actinomycosis, and in leukemic proliferation.

Another characteristic of radiation which is of general importance to medicine is its influence upon the endocrine glands, whose action, especially in a morbidly increased condition, by radiation can be reduced, and possibly, under favorable conditions, restored to normal function. Through this influence of radiation upon the endocrine glands radiotherapeutics is enabled to act upon the entire organism. I need only remind you of its tried influence upon the thyroid gland in the case of *morbus basedowii,* upon the pituitary gland in acromegaly, and upon the ovaries in menorrhagia. Through its action upon the endocrine apparatus radiotherapeutics also possesses a chance of influencing the conditions for benign and malignant tumors in the body. In this connection I wish only to remind you of the influence of ovarial radiation upon fibromyomas and upon mammary cancer. It is probable that we are here face to face with fresh possibilities for radiotherapeutics.

Its greatest importance radiotherapeutics has, however, attained through direct radia-

tion of tumors. All other conquests of therapeutics are far surpassed by the fact that for the *first time in the history of medicine it has been possible to produce a healing process in malignant tumors,* a healing process which in several forms of tumors may bring about a complete healing of the tumorous disease without any mechanical removal of the tumor. From being able at the start to overcome only minor, comparatively benign formations in the skin, radiotherapeutics now forms an important aid to surgery in the treatment of cancer, and is able in the case of certain tumors to attain better and safer results than surgery. Thorough and extensive investigations have also made manifest the important fact that a cure of cancer by radiotherapeutics is permanent to an extent at least equal to that after a radical operation. On the other hand, radiotherapeutics with our present technics appears to exercise only a local effect upon tumors, so that a prospect of a permanent cure exists only in the case of locally restricted cancerous tumors.

The advance of modern surgery by reason of aseptics during the last century has brought about the establishment of the surgical clinic and the surgical special clinics. The present century has endowed medicine with the radiotherapeutic clinic and the radiotherapeutic special clinic. The chief cause of the origin of the former is the definite experience that efficient radiotherapeutics in the case of malignant tumors is possible only at a clinic and policlinic especially established for the purpose, in charge of medical men who have been specially trained in this branch of therapeutics and are devoting themselves entirely to it.

Radiotherapeutics and roentgen diagnostics possess a wide and common basis in the largely joint roentgen physics and roentgen technics. At the public hospitals they also form, for economic and practical reasons, an organic whole in charge of a medical practitioner trained in both branches of radiology.

As a scientific sphere of research roentgen therapeutics is, on the other hand, as to its nature as different from roentgen diagnostics as, by way of example, heliotherapeutics in its scientific task differs from microscopic anatomy.

In the earlier stages of development of roentgen diagnostics, when the technics had yet to be developed step by step, the bulk of the work done by roentgenologists was devoted to technical tasks. Roentgen diagnostics in those days could be called only a research method. Since roentgen technics have reached a higher level of development, and since at most places better possibilities for scientific research have been provided, the purely diagnostic task forms the bulk of roentgenologists' scientific and practical work.

Medical roentgen diagnostics has developed into a science—the science relating to the structure of the human body as it appears on investigation by means of the roentgen ray. It is a branch of normal and pathologic anatomy, and is in its nature very closely allied with microscopic anatomy. In the same way as anatomy and pathology, roentgen diagnostics is an auxiliary science of practical medicine. Nevertheless, in its use it occupies a distinct position toward the theoretical medical disciplines, necessitated by the fact that roentgen diagnostics is carried out upon live human beings. The roentgenologist, in his capacity of physician, comes in contact with the sick individual, and his examination must be planned individually with regard to the disease symptoms in each case, and in evaluating the observations made in the course of the roentgen examination. Although roentgen diagnostics in respect of its working methods and objects under examination is a branch of anatomy, it forms nevertheless a *clinical* or policlinical discipline, which calls for an

institution established with regard to the same. Roentgen diagnostics occupies a distinct position also by virtue of the fact that it is practised with special technics, which for delicate or thorough examination call for a more complicated and extensive instrumentarium. Roentgen technics have, however, been specialized not only by their instruments but also by the fact that the result of investigation in every complicated instance is entirely dependent upon the planning of the investigation and its consequent performance.

Roentgen diagnostics deviates from ordinary anatomy also by the special character of the roentgen picture. In fact, as is well known, the roentgen picture does not form a reflection of the outer and inner organs such as they appear to the naked eye when laid bare. It forms a central projected picture, which at the same time registers the differences in density of the structure of the organs depicted. In other instances, again, the roentgenograms supply projected pictures of the inner surfaces of the hollow organs, after casts of the latter have been produced by artificially introduced contrast media.

In many instances the projected pictures of disease processes certainly coincide with the pictures of corresponding changes known to the eye, but in the majority of cases the roentgenograms, in order to supply reliable information, must be carefully analyzed and judged with respect to the technic employed, and with a knowledge of the normal and pathologic roentgen anatomy.

The importance of roentgen diagnostics to medical science is undoubtedly at the present day perfectly obvious not only to representatives of medical science but also to every erudite man or woman. Roentgen diagnostics is now indispensable for investigating a large number of diseases. From year to year its duties are growing greater and greater, and the surety of the results is augmented.

Vast and important fresh tasks await the roentgenologist both within the sphere of roentgen anatomy and roentgen pathology and in clinical roentgen diagnostics. Thus we are only on the threshold of a knowledge of the normal and pathologic mechanism of motion of the alimentary canal. As to the roentgen anatomy and pathology of the lungs and heart we have, thanks to the progress of technics, to expect fresh and important knowledge. Through refined and improved methods of investigation by means of contrasting agents roentgen anatomy of the urogenital apparatus and the gall bladder is rapidly developing. Diagnostics in the sphere of the bone system and roentgen diagnostics of changes in the subcutaneous and subperitoneal connective tissues are about to pass from purely rough anatomical studies into a science which approaches the borders of histology, inasmuch as the improved sharpness of roentgenograms enables the study of the same in multiple enlargement.

In a still higher degree than radiotherapeutics roentgen diagnostics has set its seal upon present-day medical science. A roentgen diagnostic department in charge of an expert is a necessary portion of every modern hospital.

By reason of its scientific and practical importance, therefore, radiology at the present moment is entitled to the independent position in scientific and practical work which accrues to other medical methods. It is for us radiologists a precious duty in every way to try to make ourselves worthy of the place in the sun which we demand for our science. The only way to attain it is by conscientious research and scientific tuition. Teaching and training in radiology have hitherto in most countries not kept abreast of the development of radiology in

practical medical science. The organization of training is at the present the main question of radiology, and the chief subject at this world's congress.

THE ANNUAL MEETING

TENTATIVE PROGRAM

Opening of the Scientific Session, Monday, December 3, 1928

A. Symposium on X-ray Unit Standardization Problems.
B. Miscellaneous X-ray and Radium Therapy Papers.
C. Meeting of the Counselors.
Executive Session.
Reports of Committees.

Tuesday, December 4, 1928

Section A. X-ray Therapy and Physics.
Section B. X-ray Diagnosis.
Digestive Tract.
Bone System.

SYMPOSIUM: "Ultra-violet Light"
DR. A. U. DESJARDINS, *Leader,* Mayo Clinic, Rochester, Minn.
DR. EDGAR MAYER, Saranac Lake, New York
(Subject to be announced.)
DR. HORACE LO GRASSO, Perrysburg, New York
(Subject to be announced.)
DR. HEUER, Professor of Surgery, University of Cincinnati
(Subject to be announced.)
DR. WILLIAM T. ANDERSON, Jr., Hanovia Chemical and Manufacturing Company
(Subject to be announced.)
DR. WILLIAM T. BOVIE, Professor of Biophysics, Northwestern University
(Subject to be announced.)

SYMPOSIUM: "Cholecystography"
DR. EVARTS A. GRAHAM,
DR. WARREN H. COLE,
DR. GLOVER H. COPHER,
DR. SHERWOOD MOORE, St. Louis, Mo.

SYMPOSIUM: "Cancer of Uterus and Adnexa"
DR. ALBERT SOILAND, *Leader,* Los Angeles, Calif.
DR. FRANCES A. FORD and DR. DELLA G. DRIPS, Mayo Clinic, Rochester, Minn.
"Studies, Clinical and Experimental, with Low Dosage Irradiation for Ovarian Dysfunction."
DR. W. S. LAWRENCE, Memphis, Tenn.
"Standardization of X-ray and Radium Treatment of Carcinoma of the Cervix."
DR. W. A. NEWMAN DORLAND, Chicago, Ill.
"The Value of Radiation Therapy in the Post-operative Treatment of Papillary Cystadenoma of the Ovary."
DR. HAROLD SWANBERG, Quincy, Ill.
"The Regaud Technic of Radium Therapy in Cervical Cancer."
DR. HARRY H. BOWING and Associates, Mayo Clinic, Rochester, Minn.
"Cancer of the Rectum."

ILLINOIS NIGHT
President of Section on Radiology, Illinois State Medical Society.
President of Illinois Radiological Society.
President Chicago Roentgen Society.
Program to be arranged.

Wednesday, December 5, 1928

Section A. X-ray Therapy.
Section B. X-ray Diagnosis.

SYMPOSIUM: "Cancer Therapy, with Special Reference to Relative Radiosensitivity of Tumors."
Dr. Douglas Quick, *Leader*, and Staff of Memorial Hospital, New York City.
G. Failla, D.Sc.
"Measurement of X-ray Dosage by Physical Means."
Edith H. Quimby, M.A.
"The Skin Erythema for Combinations of Gamma- and X-rays."
Dr. James Ewing
"Radiosensitivity and Selective Action of Different Types of Radiation."
Dr. Frank Adair
"The Response of Various Types of Breast Cancer to Radiation."
Dr. William P. Healy
"Variations in Radiosensitivity of Epidermoid Carcinomas of the Cervix Uteri."
Dr. R. E. Herendeen
"Radiation in Primary and Metastatic Bone Tumors."
Dr. Hayes E. Martin
"Interstitial Radiation."

SYMPOSIUM: "Cancer of Prostate and Rectum"
Dr. Hugh Young and Associates, Johns Hopkins University, Baltimore, Md.

CHICAGO NIGHT PROGRAM:

1. President Max Mason of University of Chicago.
   "Radiology in the University."
2. Professor Bovie of Northwestern University.
   "Radiology and the Living Cell."
3. Professor Arthur Compton and Professor William D. Coolidge.
   Subjects to be announced.

Thursday, December 6, 1928

Section A. X-ray Therapy, Biological and Physical Problems.
Section B. X-ray Diagnosis.
SYMPOSIUM: "Cancer of the Rectum"
Dr. Harry H. Bowing and Associates, Mayo Clinic, Rochester, Minn.
SYMPOSIUM: "Cancer of the Stomach."

Annual Banquet

Address by the Retiring President.
Convocation:
Conferring of Gold Medal on Professor Arthur H. Compton of the University of Chicago.
Introduction of the newly elected officers.
Music and dancing.

Friday, December 7, 1928

Section A. X-ray Therapy, Physics, and Biological Subjects.
Section B. X-ray Diagnosis.
SYMPOSIUM: "Cancer of the Breast"
SYMPOSIUM: "Chest Diagnosis."

Approximately a hundred individual contributions have been promised, including those by the following essayists:

Digestive Tract

Dr. Richard Hayes, Longview, Wash.
"Intermittent Duodenal Stenosis."

Dr. P. B. Goodwin, Peoria, Ill.
"Diverticulum of Esophagus, with Report of Case."

Dr. Maurice F. Dwyer, The Mason Clinic, Seattle, Washington.
"Interpretation of Gastric Symptoms: A Clinical and Roentgenological Study of 3,500 Cases."

Dr. Fred M. Hodges, Richmond, Va.
"The Roentgen Ray in the Diagnosis of Mucous Colitis."

Cholecystography

Dr. James T. Case, Battle Creek, Mich.
"Reactions to the Use of Tetraiodophenolphthalein and Similar Salts for Cholecystography."

Dr. C. S. Oakman, Muncie, Ind.
"The Significance of a Faint Shadow in Cholecystography."

Dr. Lester Levyn, Buffalo, N. Y.
"Further Studies on the Absorption of Tetraiodophenolphthalein from the Alimentary Tract."

X-ray and Radium Therapy, and Physics

Dr. M. J. Sittenfield, New York.
"Prognosis of Cancer."

Dr. Ira I. Kaplan, Bellevue Hospital, New York City.
"X-ray Therapy in the Treatment of Acute Gonorrheal Arthritis."

Dr. Henry Schmitz, Chicago, Ill.
(Subject to be announced.)

Dr. Vernor M. Moore, Grand Rapids, Mich.
"Radiation Sensitization, with Case Report."

Dr. R. T. Pettit, Ottawa, Ill.
"The Use of Small Amounts of Radium at a Distance in the Treatment of Carcinoma of the Mouth and Face."

Dr. Mary Elizabeth Hanks, Chicago, Ill.
"The Roentgen Ray in the Treatment of Benign Gynecologic Cases; A Brief Summary of Twelve Years' Experience."

Dr. Alden Williams, Grand Rapids, Mich.
"A Report of Technic and Results in Treatment of Five Hundred Superficial and Borderline Malignancies, Including a Group of Eighty-five Lip Cases."

Dr. John Remer and Dr. Webster W. Belden, New York Hospital, New York, N. Y.
"The X-ray Diagnosis and Treatment of Thyroid Disease."

Dr. John J. Burby, Madison, Wis., and Dr. M. W. Barry, Omaha, Neb.
"Comparative Measurements of the Quality of Roentgen Rays."

Dr. B. H. Orndoff, Chicago, Ill.
"Radiotherapy and Electrosurgical Practice Combined."

Dr. P. M. Hickey and Dr. E. A. Pohle, with the collaboration of Dr. G. A. Lindsay and Dr. J. M. Barnes, Ann Arbor, Mich.:
"Skin Tolerance Doses in Roentgen Units and Their Relation to the Quality of Radiation."

Dr. E. D. Crutchfield, San Antonio, Texas.
"The Combined Effect of X-rays and Ultra-violet Light (An Experimental Study on Laboratory Animals)."

Dr. A. Mutscheller, Long Island City, N. Y.
"Average Wave Length of White X-ray Beams."

Dr. Ernst A. May, Newark, N. J."
"Roentgentherapy in Acute Inflammatory Conditions."

Dr. P. R. Casellas, Chicago, Ill.
"A Roentgenological Study of the Child's Chest."

Dr. W. C. Danforth, Evanston, Ill.
"The Treatment of Non-malignant Uterine Bleeding by Irradiation."

Dr. Albert Bouwers, Chief of the X-ray Department, Research Laboratory, Phillips Glolampworks, Ltd., Eindhoven, Holland.
"Self-protecting X-ray Tubes and Their Influence on the Development of X-ray Technic."

J. L. Weatherwax, M.A., and Dr. B. F. Widmann, Philadelphia, Pa.
"Physical Factors in Radiation Therapy and Their Clinical Application."

Dr. Friedrich Dessauer, Frankfort, Germany.
"About the Fundamental Biological Reaction of Radiation."

Dr. George E. Pfahler and Dr. B. P. Widmann, Philadelphia, Pa.
"Saturation Method of X-ray Treatment."

Chest

Dr. John T. Farrell, Philadelphia, Pa.
"The Roentgen Appearance of Primary Carcinoma of the Bronchus."

Dr. R. P. Potter, Marshfield, Wis.
"Diagnosis of Intrathoracic Tumors."

Dr. Leon T. LeWald, New York University, New York.
"Chronic Lung Suppuration: Report of Three Cases of About Ten Years' Duration."

Dr. Karl Kornblum, University Hospital, Philadelphia, Pa.
"Post-operative Atelectasis, with Special Reference to the Lobular Type."

Dr. Samuel Brown, Cincinnati, O.
"Radiology of the Thorax: A Study of the Thorax in Three Dimensions."

Dr. I. Pilot, Chicago, Ill.
"Mesenchymatous Tumors of the Lung and Pleura."

Bone System

Dr. Wilbur H. Gilmore, Chicago, Ill.
"Fractured Pelves."

Dr. James A. Evans, LaCrosse, Wis., and Dr. E. Evans, Minneapolis.
"Osteitis Fibrosa Cystica."

Dr. M. A. Bernstein, Chicago, Ill.
"Metastatic Invasion into Synovial Membranes and Bones."

Dr. John A. Beals, Jacksonville, Fla.
"An Intracranial Calcification, Probably of Choreoid Plexus."

Dr. Howard P. Doub, Detroit, Mich.
"Report of a Hip Condition of Undetermined Etiology."

Dr. W. W. Wasson, Denver, Colo.
"The Incipiency of Disease."

Dr. W. M. Storey, Madison, Wis.
"Importance of Thorough Oral Diagnosis."

Dr. Sidney A. Portis, Chicago, Ill.
(Subject to be announced.)

Dr. E. G. C. Williams, Danville, Ill.
(Subject to be announced.)

Dr. Fred Hodges, Madison, Wis.
"The Diagnostic Department of a General Hospital."

Dr. E. C. Franing, Galesburg, Ill.
(Subject to be announced.)

Dr. J. Newton Sisk, Madison, Wis.
(Subject to be announced.)

Dr. P. M. Hickey, Ann Arbor, Mich.
"The Pathological Larynx."

Dr. C. B. Rose, Chicago, Ill.
(Subject to be announced.)

Dr. C. E. Cook and Dr. Walter Theobauld, Chicago, Illinois.
"Report on Accessory Sinuses with Opaque Media, with Operative Findings."

Dr. I. S. Trostler, Chicago, Ill.
(Subject to be announced.)

Dr. Malcolm B. Hanson, Glen Lake Sanatorium.
(Subject to be announced.)

Dr. Max Kahn, Baltimore, Md.
(Subject to be announced.)

Dr. A. C. Ivy, Professor of Physiology, Northwestern University.
"The Newer Physiology of the Gall Bladder."

Dr. B. C. Cushway, Chicago, Ill.
"The Anatomical Variations Found in the Symptomless Spine and Their Application to Industrial and Medicolegal Work."

Dr. J. Thompson Stevens, Montclair, N. J.
"Cervical Carcinomata."

Dr. O. M. Walter, Chicago, Ill.
"Hypoparathyroidism as a Complication of Thyroid Surgery."

CLINICS

Clinics are being arranged along the following lines:

Experimental Clinical Work.—In the medical schools of the University of Illinois and of Northwestern University.

Interpretation Clinics.—In the medical schools of the University of Illinois, the University of Chicago, and Northwestern University; also in Wesley and Cook County hospitals.

Clinical Case Demonstrations.—At the Municipal Tuberculosis Sanatorium and at Cook County and St. Luke's hospitals.

Dr. Bloodgood's Clinics.—These will cover the subjects of tumors of the periosteum and of bone.

Clinics at the Hotel.—These will be conducted by Dr. Lewis Gregory Cole, Dr. E. S. Blaine, Dr. B. C. Cushway, Dr. Amédée Granger and others, and will consist of demonstration of cases and interpretation and discussion of films.

BOOK REVIEWS

ELEMENTS DE LA PHYSIQUE DES RAYONS X. INTRODUCTION A LA RADIOLOGIE MEDICALE ET A L'ETUDE GENERALE DES RAYONNEMENTS. By F. WOLFERS. Pages, 336. Published by J. Hermann, Paris, 1927. Price 25 francs.

This is a compilation of six lectures concerning the physics of X-rays. The following subjects are discussed: Deep X-ray therapy, diffraction and spectra of X-rays, the quantum theory, secondary radiation, absorption, methods of measurement, apparatus, electrons and X-ray tubes.

The subjects are exceedingly well presented. They are, however, quite technical and will not appeal to the average radiologist.

THE NEW YORK ACADEMY OF MEDICINE LECTURES ON MEDICINE AND SURGERY. First series, 1927. Pages 319. Paul B. Hoeber, Inc., New York, 1928. Price $5.00.

This is a compilation of the first series of Practical Lectures for the General Practitioner, arranged by the Committee on Medical Education and given at the New York Academy of Medicine during 1926-1927.

The volume contains fifteen lectures covering the following subjects: The Treatment of Cardio-vascular Syphilis; Intestinal Obstruction; Surgical Aspects of Medical Conditions; Clinical Aspects of Common Otological Infections; General Infections by Bacteria; The Cutaneous Manifestations of Syphilis; Climate in Tuberculosis; Useful Drugs in Clinical Practice; Obstetrical Problems in General Practice; Surgical Aspects of Diseases of the Thyroid; The Treatment of Pneumonia; Pathologic Causes of Human Misconduct; Remarks on Eye Conditions; Contagious Diseases.

The material is presented by many well known metropolitan specialists. The lectures are well arranged and are fully illustrated. The general practitioner will find much of value in this book.

HANDBUCH DER GESAMTEN STRAHLENHEILKUNDE, BIOLOGIE, PATHOLOGIE UND THERAPIE. Edited by DR. PAUL LAZARUS. Erster Band. Verlag von J. F. Bergmann, München, 1927. Pages 166. Price 16.5 marks.

This is a rather technical presentation of the physical principles of radiation. The subjects are arranged in four parts. In Part I Lazarus discusses the new methods and indications for radiation. Part II, by Sommerfeld, concerns atoms, electrons, ions, and radiant energy. In Part III Dorne describes the physical basis of sun and light therapy. The therapeutic properties of radio-active substances and their rays are discussed in Part IV by Hahn.

The material is well presented but the bibliography, which is a valuable part of a work of this sort, has been omitted from all but Part III. This volume will appeal more to the physicist and research worker than to the average radiologist.

ABSTRACTS OF CURRENT LITERATURE

INDEX TO ABSTRACTS IN THIS ISSUE

On the Present Status of Ultra-violet Radiation in Athletics. W. Hering. Strahlentherapie, 1928, XXVIII, 615.

This is a severe criticism of the general use of the quartz mercury vapor lamp in athletics. It should not be employed before contests as a means of increasing the physical efficiency of the team.

E. A. POHLE, M.D.

Modern Methods of Treatment and Results in Cancer of the Bladder. Bransford Lewis and Grayson Carroll. Texas State Jour. Med., January, 1928, p. 574.

As illustrating the modern methods of attacking cancer of the bladder a case is briefly cited. An obviously cancerous tumor of the bladder, proven by biopsy to be carcinoma, was first treated by fulguration down to its base; then 50 mgm. of radium element was applied to the ulcerated area, held in place by means of a wire applicator; later a series of high voltage X-ray treatments were applied. This patient, treated in 1919, is still well, without sign of recurrence. In a general way, all such lesions are similarly treated, except that radium emanation is implanted instead of held by a capsule of radium element in contact with the lesion. Histories of eight patients are given, all of them successfully treated.

W. WARNER WATKINS, M.D.

The Healing of Gastric Ulcers: Radiological Observations. F. G. Nicholas and Alan Moncrieff. Brit. Med. Jour., June 4, 1927, p. 999.

This paper gives the results of investigation of a group of cases by means of repeated opaque meals over a period of two years, using the "double meal" and "rotation methods."

It was concluded that—

(1) The disappearance and reappearance of the characteristic "niche" were associated, respectively, with remission and recurrence of clinical symptoms and signs.

(2) There is no relation either between the length of the history or the size of an ulcer, and the rate or permanence of healing.

(3) There are certain fallacies, such as disappearance of the "niche" due to filling with food, mucus, scar tissue, etc., but on the whole radiological investigation of healing is a most valuable method.

W. D. MACKENZIE, M.D.

A Simplified Method of Examining the Patency of the Fallopian Tubes. I. Seth Hirsch. Jour. Am. Med. Assn., Feb. 11, 1928, XC, 458.

Until now the methods for the determination of the patency of the Fallopian tubes have utilized the injection of gas and such contrast mediums as iodized oil, bismuth, or barium emulsions. No matter how carefully these substances are introduced into the uterine cavity, it is practically impossible to avoid producing a positive intra-uterine and intratubal pressure. Not that such pressure is harmful, but it does not give in exact terms the state of actual patency of the tubes. The author has devised a method in which only the natural motive forces operative in the uterotubal canal carry the contrast medium through the Fallopian tubes.

Bismuth is rubbed up with just enough petrolatum and oil of theobroma to render it pliable. The mass is then pressed by means of a mold into the form of suppositories and cut into pieces 3 cm. long and 2 mm. thick. The bismuth content is about 75 per cent. At the body temperature the suppository melts and the contrast salt then exists in a suspension of petrolatum and oil of theobroma. The suppositories are introduced into the uterus by means of a cannula of 4 mm. caliber, and wire trocar.

Immediately after examination the uterus is outlined, not as a dense shadow but as a linear triangular shadow branching at a point corresponding to the fundus. The proximal portion of the tube shows as a simple, fine line, corresponding to the isthmus, and a wider linear shadow corresponding to the ampulla and segmentation, depending on the extent of tubal peristalsis. Examination one hour after insertion may show the contrast substance outlining the tubes, or the granules may be at the fimbriated end of the tube or in the peritoneal cavity. Several days later the shadows of the contrast salt can no longer be visualized. A single examination two hours after the insertion of the suppository is sufficient to determine whether or not the tubes are patent.

The rapidity with which the contrast substance is carried to the tubes makes it highly improbable that its movement is due to action of the ciliated epithelium of the uterine mucosa. It is probable that a uterine contraction brings the contrast substance to the tube and tubal peristalsis carries it to the fimbria and out, although experiments on animals have shown that particles of contrast substance do not find their way into the Fallopian tubes unless there is a free communication between the tube and the peritoneal cavity, suggesting that a purely mechanical factor such as aspiration may be at play in the mechanism.

This method may be practised without the slightest inconvenience to the patient.

The Roentgenologic Manifestations of Primary Carcinoma of the Lung: I.—Parenchymal Type. B. R. Kirklin and Ralston Paterson. Am. Jour. Roentgenol. and Rad. Ther., January, 1928, XIX, 20.

The authors present the roentgen findings in early cases of primary carcinoma of the lung. They find three roentgenologic types: the nodular, showing a single irregularly circular nodule with infiltrating edges; the lobar, showing a homogeneous consolidation of a lobe with infiltrating edges, and the hilar, showing an increased density of the bronchial tree radiating from the hilum. The last type is very apt to be confused with a primary bronchial carcinoma, and in such cases a bronchoscopic examination is necessary for differentiation. It is the writer's belief, however, that all three types arise as a single pulmonary nodule, so that, if seen early enough, all cases would appear as the first type. The differential diagnosis between primary carcinoma in its several manifestations and metastatic malignancy and lung abscess is often exceedingly difficult.

J. E. Habbe, M.D.

Wood's Glass and the Detection of Ringworm by Its Fluorescent Properties. N. Gray Hill. Brit. Jour. Child. Dis., January-March, 1928, XXV, 54.

The author states that a glass known as Wood's Glass or Chance's U. V. Glass is used at Queen Mary's Hospital for Children, Carshalton. In appearance it is about the thick-

ness of ordinary window glass and of a deep violet color. It transmits only the shortest rays of the visible spectrum and between 70 and 80 per cent of the ultra-violet in the region between 4,000 and 3,000 A.U.

The method used at Carshalton is to have a small piece of Wood's Glass, about two inches square, in an applicator that can be fixed in front of the window of a Kromayer lamp. The room in which the examination is carried out should be darkened, but should not be too dark, as this tends to frighten children and so delay the work. The patient should be seated in a chair and the lamp should be held two or three inches from the scalp; it can be easily manipulated with one hand, leaving the other free to brush up the hair. If infected (*Trichophyton microsporon* only type investigated), the infected hairs will light up as they come under the rays of the lamp and become a most vivid green color. The scalp and uninfected hairs are only just illuminated by the purple light. The author states that vaseline, brilliantine and other ointments fluoresce in a striking manner, but the color is an electric blue, while with ringworm the color is a vivid green.

In conclusion, the author states it may fairly be claimed that the use of Wood's Glass gives us an easy and certain method of diagnosing ringworm, even in the earliest stages. What is almost of equal importance, the method provides us after-treatment, with a ready method of telling when a child is cured and fit to mix with his fellows. Systematically used it should lead in the immediate future to the stamping out of ringworm.

B. C. CUSHWAY, M.D.

Increase of Resistance to Streptococcal Sepsis by Roentgen Rays in an Animal Experiment. F. Bass and K. Jaroschka. Strahlentherapie, 1928, XXVIII, 568.

Since the inauguration of the roentgen-ray treatment of inflammatory diseases, the possibility of influencing sepsis in the same way has suggested itself. The authors studied this problem on rabbits and guinea pigs, which were treated with 325 to 350 *R* or about 5 to 6 *H* on the skin (200 K.V., 3 ma., 0.5 Zn. plus 1.0 Al., 40 cm. distance) twelve to fourteen hours before or five hours after inoculation with streptococci. It is concluded that local irradiation before or after infection does not produce immunity but definitely increases the resistance of the organism. This manifests itself in a longer life of the treated animals as compared with the untreated controls. The authors believe that the reticulo-endothelial system plays the most important rôle in the observed effect of roentgen rays on the resistance to streptococcal sepsis.

E. A. POHLE, M.D.

The Basal Metabolism in Chronic Lymphatic Leukemia. C. I. Krantz and M. C. Riddle. Am. Jour. Med. Sci., February, 1928, CLXXV, 229.

The study of the basal metabolism and the formed elements of the blood in 31 cases of chronic lymphatic leukemia is reported, and the following conclusions reached: The basal metabolic rate is elevated when the leukemic process has progressed far enough to cause other than local symptoms. The symptoms are due to this elevated rate rather than to the presence of the increased number of white cells. The rise in the basal metabolic rate or in the symptoms is not closely related to the white count when a group of cases is considered, although in individual cases there may be a simultaneous drop following irradiation. The authors usually use 500 *e*-units at a sitting. They treat locally only when pressure symptoms are present. A dose of 250 to 500 *e*-units often produces a marked decrease in the leukocyte count. A short transitory rise in the basal metabolic rate is usually noted within three days but this later drops. The number of platelets present tends to bear an inverse relationship to the basal metabolic rate.

Patients should be treated only when the proper indications are present, such as (1) elevated basal metabolic rate; (2) white blood count over 100,000; (3) symptoms of pressure, although at times it is advisable to

irradiate when the count is over 100,000 and the basal metabolic rate is low.

Contra-indications: (1) when the bone marrow is involved so that there is marked anemia; (2) when the circulating blood contains large numbers of immature lymphocytes; (3) when the platelet count is below 60,000; (4) when recent adequate therapy has not benefited the patient; (5) when conditions exist which in general indicate caution in the use of radiography, as chronic nephritis, diabetes, large doses over the same area, etc. A leukopenia is usually considered a contra-indication, but when this is present with a high basal metabolic rate or pressure symptoms, full doses of roentgen rays can be given with safety and benefit. The determination of the basal metabolic rate is of more value in the indication of treatment than the white blood count.

R. A. Arens, M.D.

Report of Thirty-one Cases of Therapeutic Abortion Induced by Roentgen-ray Therapy. Samuel Stern. Am. Jour. Roentgenol. and Rad. Ther., February, 1928, XIX, 133.

Thirty-one pregnant women, all poor surgical risks, each with some chronic ailment which made abortion absolutely essential, were given roentgen-ray therapy in preference to surgery to produce an emptying of the uterus. The duration of pregnancy varied from four weeks to three and one-half months. The fetus was expelled spontaneously in twenty-six cases, twenty-one of these intact in the sac and five separately. Of the remaining five cases, two were curetted seven and nine weeks, respectively, after roentgen therapy and in both cases a fetus which had been dead some time was found. The third case had a hysterectomy performed thirty-two days after roentgen therapy and in this case also a dead fetus was obtained. Of the two remaining cases, one following X-ray therapy without spontaneous abortion, when curetted, showed degenerative changes in the chorionic villi; the other was an apparent failure (due to under-dosage), since the uterus continued to enlarge for two months following therapy, at which time labor was surgically induced.

The majority of cases were treated through two portals, one anteriorly and one posteriorly, the aim being to apply to the uterus about 50 to 60 per cent of a skin unit dose. Copper filtered penetrating rays were used.

Practically all of the patients showed some signs of castration and a persistent amenorrhea a year after abortion had been induced. However, the author feels that very probably these results can be avoided by varying the dosage and the technic of administration. After gestation has proceeded beyond four to four and a half months, roentgen therapeutic abortion may not be nearly as effective as in the earlier months.

J. E. Habbe, M.D.

Biological Effects of Roentgen Rays Studied in the Chicken from the Ovum to the Explanted Organ. Konrad Heim. Strahlentherapie, 1928, XXVII, 694.

The administration of small doses of roentgen rays to the ovaries and the performance of a temporary sterilization have brought up the problem of injury to the offspring. The author studied this problem on chicken eggs with the following technic: 200 K.V., 0.8 Cu. plus 1.0 Al., 4 ma., 30 cm. F.D., E.D. equal to 500 *R*, or 19 minutes. He found that the exposure of fecundated chicken eggs to 500 *R* of hard roentgen rays, carried out immediately before artificial hatching, led to marked injuries of the offspring. The degree of injury seemed to be dependent upon the dose. Similar injuries were observed if the exposure took place during the first days of hatching. The morphological effect decreased with increasing age of the exposed embryos. The explantation experiments with tissue of irradiated embryos did not lead to uniform results. Irradiation of the ovary of the hen stopped temporarily the laying of eggs. When it started again no injuries to the embryos hatched from such eggs could be detected over a period of five months. The possibil-

ity of idiokinetic injuries could not be ruled out by these experiments.

E. A. Pohle, M.D.

A Case of Achalasia of the Cardia in a Child of Seven Years. W. Gordon Sears. Brit. Jour. Child. Dis., January-March, 1928, XXV, 48.

The author reports a case of achalasia, or cardiospasm, in a child seven years of age. He had made his diagnosis upon history of vomiting for eight or nine months, loss in weight, and X-ray examination of the esophagus. He treated this case with Hurst's achalasia "mercury bougie," size 24, which was passed three times a day and allowed to remain in position for 15 minutes, immediately after which feeding of one-half pint of egg and milk was given. The following day there was no vomiting. This treatment was continued for nine days and then the time decreased to 10 minutes. At the end of fifteen days practically no residue was left in the esophagus after the liquid meal. X-ray examination at the end of thirty days showed no residue in the esophagus, which appeared to be less dilated. The author reports a recurrence in about four months' time, as the patient had refused to pass the "bougie." When this was resumed the patient had no more vomiting and continued to gain weight.

Following this report is a brief résumé of other cases in the literature, and methods of treatment.

The case reported, according to Dr. Sears, is the first case of this type in a child to be treated with "mercury bougie," although this method is often employed in adults.

B. C. Cushway, M.D.

Perforated Ulcer Simulating Diverticulum of the Stomach. Eugene Freedman. Am. Jour. Roentgenol. and Rad. Ther., July, 1927, XVIII, 47.

The author reports a case, accompanied by drawings, of a perforated ulcer of the stomach in the region of the cardia and on its posterior wall. The clinical picture presented by the patient was that of carcinoma of the pylorus, and the roentgen findings of a large pouch about seven centimeters in diameter, the lower anterior quadrant of which presented an irregular margin, with six- and eighteen-hour retention in the sac, suggested gastric diverticulum, with possible malignant degeneration of its wall.

Operative effort to resect the supposed diverticulum failed, and the patient died on the ninth day post-operative. The autopsy findings proved the condition to be a perforated gastric ulcer associated with a benign adenoma of the stomach and perigastric abscess formation.

J. E. Habbe, M.D.

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